A COMPARATIVE STUDY OF DIAGNOSTIC VALUE OF HYPERBILIRUBINEMIA IN PREDICTING APPENDICITIS AND ITS COMPLICATIONS

A DISSERTATION SUBMITTED TO THE TAMILNADU
Dr. MGR MEDICAL UNIVERSITY
CHENNAI
In partial fulfillment of the Regulations
For the award of the Degree of
M.S. (GENERAL SURGERY) BRANCH-I

DEPARTMENT OF GENERAL SURGERY
MADURAI MEDICAL COLLEGE
MADURAI

MAY 2019

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY OF DIAGNOSTIC VALUE OF HYPERBILIRUBINEMIA IN PREDICTING APPENDICITIS AND ITS COMPLICATIONS**" is a bonafide research work done by **Dr. SANJU UNNIKRISHNAN,** M.S. Postgraduate student in the Department of General Surgery, Madurai Medical College & Hospital, Madurai, in partial fulfillment of the requirement for the degree of M.S. in GENERAL SURGERY.

Date
:

Place: Madurai

Dr. P. AMUTHA, M.S.,
Professor,
Department of General Surgery,
Madurai Medical College,
Madurai

CERTIFICATE BY THE HEAD OF THE DEPARTMENT

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY OF DIAGNOSTIC VALUE OF HYPERBILIRUBINEMIA IN PREDICTING APPENDICITIS AND ITS COMPLICATIONS**" is a bonafide research work done by **Dr. SANJU UNNIKRISHNAN, M.S.** Postgraduate student in the Department of General Surgery, Madurai Medical College Madurai, under the guidance of **Dr.P. AMUTHA M.S.,** Professor, Department of General Surgery, Madurai Medical College, GRH, Madurai in partial fulfillment of the requirements for the degree of M.S. in GENERAL SURGERY.

Date
:

Place: Madurai

PROF. Dr. S.R.DHAMODHARAN MS
Professor and HOD of General Surgery,
Department of General Surgery,
Madurai Medical College,
Madurai

CERTIFICATE BY THE HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY OF DIAGNOSTIC VALUE OF HYPERBILIRUBINEMIA IN PREDICTING APPENDICITIS AND ITS COMPLICATIONS"** is a bonafide and genuine research work carried out by **Dr. SANJU UNNIKRISHNAN**, under the guidance of **Dr.P. AMUTHA M.S.,** Professor, Department of General Surgery and HOD, Department of General Surgery, Madurai Medical College, Madurai.

Date
:
Place: Madurai

Prof. Dr. D.MARUTHUPANDIAN MS
DEAN
Madurai Medical College,
Madurai

DECLARATION BY THE CANDIDATE

I hereby declare that the dissertation entitled **"A COMPARATIVE STUDY OF DIAGNOSTIC VALUE OF HYPERBILIRUBINEMIA IN PREDICTING APPENDICITIS AND ITS COMPLICATIONS"** is a bonafide and genuine research work carried out by me under the guidance of **Dr.P. AMUTHA, M.S.,** Professor, Department of General Surgery, Madurai Medical College, Madurai. The Tamil Nadu Dr. M.G.R. Medical University, Chennai shall have the rights to preserve, use and disseminate this dissertation in print or electronic format for academic/research purpose.

Date
:

Place: Madurai

Dr. SANJU UNNIKRISHNAN
Postgraduate in General Surgery,
Department of General Surgery,
Madurai Medical College,
Madurai

ACKNOWLEDGEMENT

This study would have been impossible but for the enduring guidance of my eminent teacher and esteemed guide **Dr. P. Amutha MS,** Professor, Department of Surgery, Madurai Medical college, Madurai. I would like to express my sincere and heartfelt gratitude for her resolute guidance, precise approach, constructive criticism and meticulous supervision throughout the course of my work and preparation of manuscripts that have been a valuable part of my learning experience.

I express my sincere gratitude to **Dr. S.R.DHAMODHARAN, M.S,.FIAS,** Professor and Head, Department of Surgery, Madurai Medical College, Madurai, for his valuable suggestion, indispensable guidance, critical appreciation, support and affection in pursuit of this study and post-graduation.

Sincere and heartfelt thanks to all other esteemed teachers in the Department of General Surgery of Madurai Medical College, Madurai.

I am also thankful to my Assistant Professors **Dr. T. Vanitha MS, Dr. A Suganya MS, Dr. P. Vanitha MS DGO, Dr. S.Hemankumar MS** for their help.

I will be failing in my duty, if I do not express my gratitude to all the patients involved in the study. Without their co-operation the study would not have been possible. I would like to thank my parents who stood by me in every step of the way and are a constant source of inspiration.

Date:

Place: Madurai

Dr. SANJU UNNIKRISHNAN
Postgraduate in General Surgery,
Department of General Surgery,
Madurai Medical College,
Madurai

CONTENTS

INTRODUCTION

The most common cause of acute abdomen is Appendicitis. The diagnosis of acute appendicitis is based on clinical history and physical examination. It is difficult to diagnose in cases of retrocaecal or retro ileal appendix. Appendicectomy is the most commonly performed abdominal surgery. 15-30% of appendicectomy specimen found to be normal.In order to decrease the number of unnecessary appendicectomy, significance of labarotory investigations like White Blood Cells,,C-Reactive Protein, etc have been emphasised.Ultrasonagram abdomen has been widely accepted as the diagnostic tool for appendicitis.Many number of scoring system were developed to arrive the diagnosis. These scoring systems are based on clinical features, laboratory investigations. Some examples are Alvarado, Modified alvarado, Ripasa.

Still there is no definitive laboratory marker for acute appendicitis and appendicular perforations. Studies show that serum bilirubin is raised in acute appendicitis and appendicular perforations.But the siginificance of which is not stressed.On bacterial invasion of the appendix, there is transmigration of bacteria and release of proinflammatory cytokines like TNF α,.IL6 .

The cytokines reach the liver through the superior mesentric vein and may lead to inflammation, abscess and liver dysfunction.

In view of the above context, the present study was undertaken to assess the relationship between HYPERBILIRUBINEMIA and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to see whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

OBJECTIVES

The objectives of the study were-

1. To study the relationship between hyperbilirubinemia and acute appendicitis; and to evaluate its credibility as a diagnostic marker for acute appendicitis.

2. To evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

REVIEW OF LITERATURE

EMBRYOLOGY AND DEVELOPMENT

Around the beginning of the sixth week of development of embryo, the vermiform appendix and the Caecum develops from the caecal bud which arises from the antimesenteric borders of the caudal limb of the mid gut loop[2]. At this stage definite identification of the small and large intestine as separate entities occur. The out pouching maintains a conical shape until the fifth month of fetal growth, after which proximal portion expands to form the Caecum and the tip begins to elongate and develops into the vermiform appendix[31].

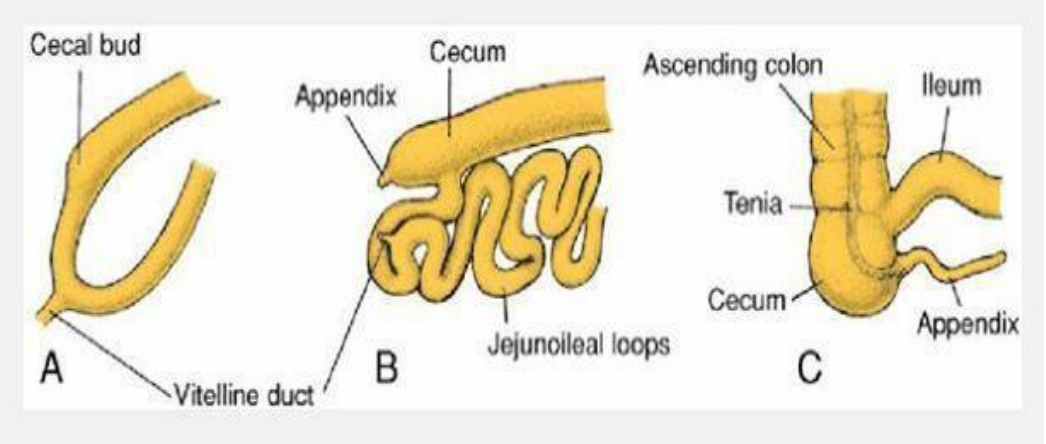


Figure 1: Successive stages in development of the caecum and appendix.

A. 7 weeks. B. 8 weeks. C. Newborn.

CONGENITAL ABNORMALITIES:

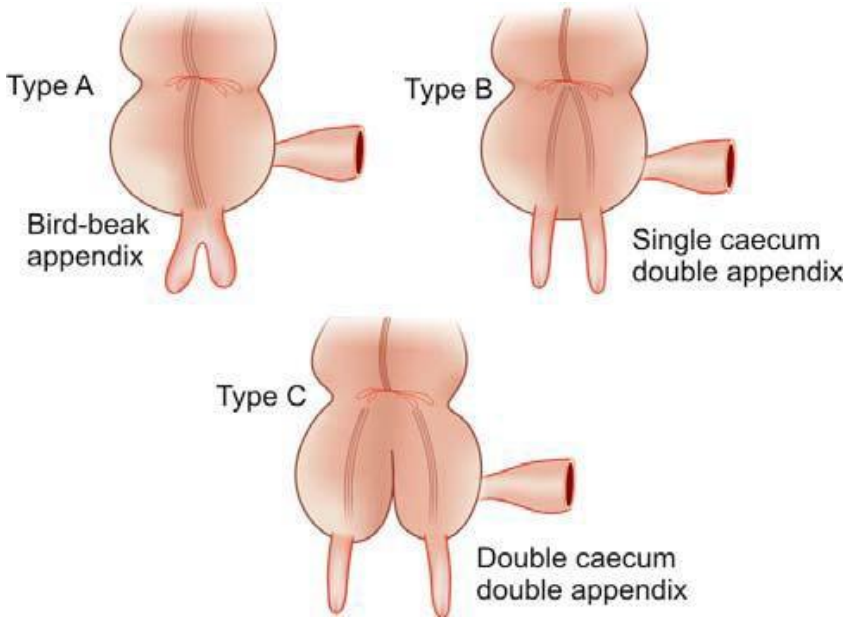
DUPLICATION OF APPENDIX

(Wallbridge Classification)

Type A: Partial duplication in a single caecum.

Type B: Two separate appendices in a single caecum.

Type C: Double caecum with each one having one appendix.



DUPLICATIONS OF APPENDIX

Various positions of appendix:

Most common position *is retrocaecal (75%). Next common is pelvic (21%).*

Other sites are:

_ Preileal—rarest (1%)

_ Postileal

_ Paracaecal

_ Subcaecal

_ Subhepatic

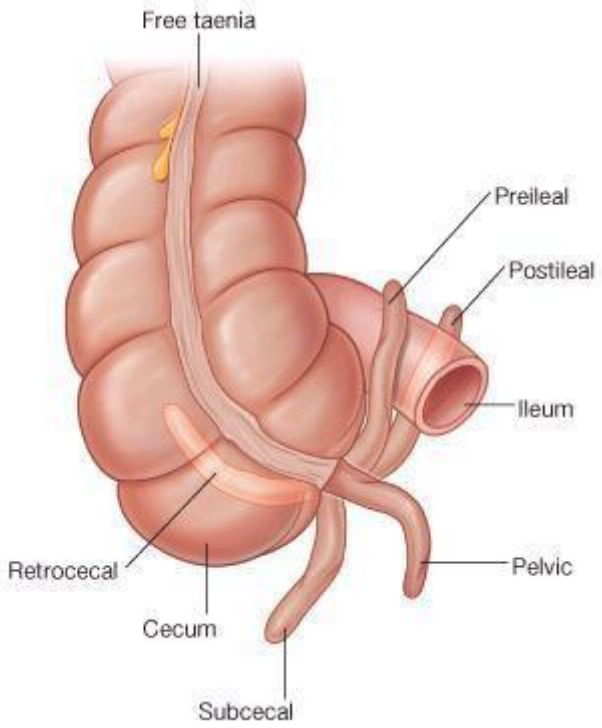


Figure 2. Various positions of appendix

Congenital diverticulum / appendicular band:

Unlike the acquired one, in this muscular layer is present.Vitelointestinal duct provides origin for some of the diverticulae and caecum may be developed from the the junction of these two structures. In this cases the diverticulum has fibrous band connection with the umbilicus.

Other than the band, a ring may be found extends upto the umbilicus known as appendiculo ovarian ligament.

ANATOMY OF VERMIFORM APPENDIX[32]

1. The appendicular situated on the posteromedial aspect of the caecum 2 cm below the ileocaecal orifice.

2. The appendicular orifice is occasionally guarded by an indistinct semilunar fold of mucous membrane, known as *'valve ofGerlacti.*

3. The orifice is marked on the surface by a point situated 2 cm below the junction of the trans-tubercular and right lateral planes

4. McBurney's point is the site of maximum tenderness in appendicitis. The point lies at the junction of lateral one-third and medial two-thirds of the line joining the right anterior superior iliac spine to the umbilicus.

It may occupy one of several positions.

1. The appendix may pass upwards and to the right. This is the paracolic or 11 O'clock position.

2. It may lie behind the caecum or colon, known as retrocaecal or 12 O'clock position. This is the commonest position of the appendix, about 65%.

3. The appendix may pass upwards and to the left. It points towards the spleen. This is the splenic or 2 O'clock position. The appendix may lie in front of the ileum (preileal) or behind the ileum (postileal).

4. It may pass horizontally to the left (as if pointing to the sacral promontory called promontoric or 3 O'clock position

5. It may descend into the pelvis called pelvic or 4 O'clock position. This is the second most common position about 30%.

6. It may lie below the caecum (subcaecal) and may point towards the inguinal ligament called as midinguinal or 6 O'clock position.

Lumen of Appendix

It is quite small and may be partially or completely obliterated after mid-adult lifeThe lumen of appendix is very narrow. There are *no villi*. The epithelium invaginates to form crypts of Lieberkuhn. Muscularis mucosae is ill defined.

Submucosa reveals many lymphoid masses. That is why it is called the *abdominal tonsil. Muscularis externa* comprises two layers. Outermost is the serous layer,

Peritoneal Relations

The appendix is suspended by a small, triangular fold of peritoneum, called the mesoappendix, or appendicular mesentery. The fold passes upwards behind the ileum, and is attached to the left layer of the mesentery. Occasionally, the mesoappendix may remain short of the apex.

Blood Supply

The appendicular artery is a branch of the lower division of the ileocolic artery. It runs behind the terminal part of the ileum and enters the mesoappendix at a short distance from its base. Here it gives a recurrent branch which anastomoses with a branch of the posterior caecal artery. The main artery runs towards the tip of the appendix lying at first near to and then in the free border of the mesoappendix. The terminal part of the artery lies actually on the wall of the appendix. Blood from the appendix is drained by the appendicular, ileocolic and superior mesenteric veins, to the portal vein...

NERVE SUPPLY:

Sympathetic nerves are derived from thoracic nine and ten segments through the coeliac plexus. Parasympathetic nerves are derived from the vagus. Referred pain of appendix is felt at umbilicus, similar to that of small intestine and testis.

Lymphatic Drainage

Most of the lymphatics pass directly to the ileocolic nodes, but a few of them pass indirectly through the appendicular nodes situated in the mesoappendix

Mesoappendix

The mesentery of the appendix is a triangular fold of peritoneum around the vermiform appendix. It is attached to the posterior surface of the lower end of the mesentery of the small intestine close to the ileocaecal junction. It usually reaches the tip of the appendix but some times fails to reach the distal third, in which case a vestigial low peritoneal ridge containing fat is present over the distal third. It encloses the blood vessels, nerves and lymph vessels of the vermiform appendix, and usually contains a lymph node.

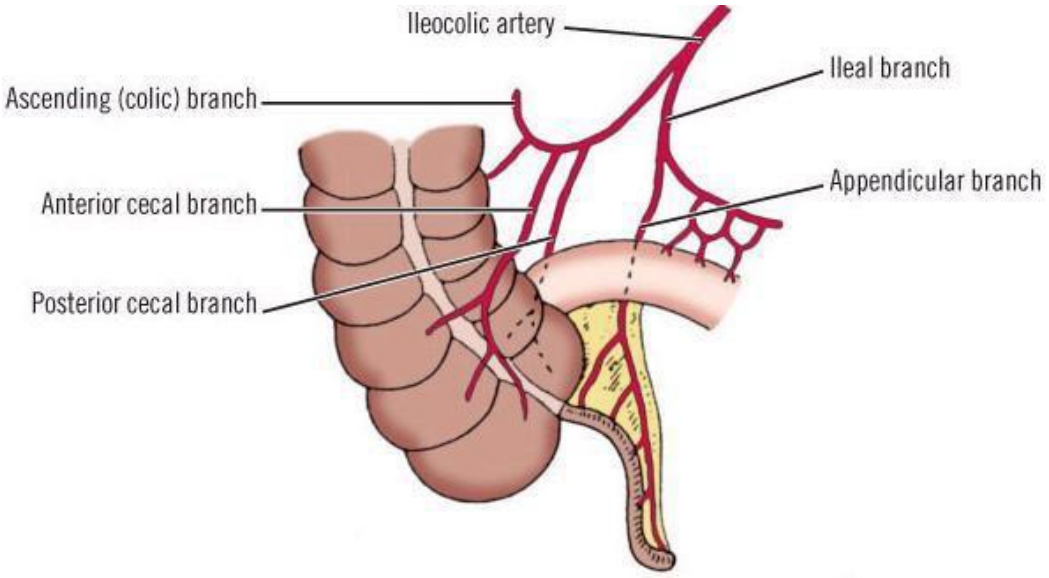


Figure 3. Blood supply of appendix

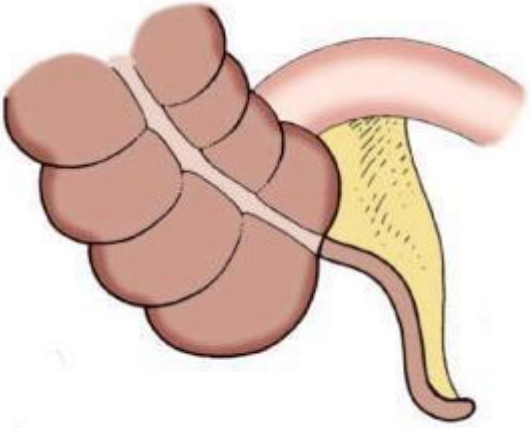


Figure 4. Mesoappendix

Caecal recesses

Several folds of peritoneum may exist around the caecum and form recesses. Paracaecal recesses are common sites for abscess formation following acute appendicitis.

Others include, Superior ileocaecal recess, Inferior ileocaecal recess and Retrocaecal recess.

Surface marking appendicular base- between the lateral and middle thirds of the straight line from the right ASIS to the umbilicus (**Mc Burney's point**),. The taenia coli converge and end on the base of the appendix.

Microstructure:

Histologically, appendix has four layers in its wall— *mucosa*, *submucosa*, *muscularis* and *serosa.* The mucosa has patchy distribution of crypts and the submucosa has abundant lymphoid tissue. Argentaffin and nonargentaffin endocrine cells are present in the base of mucosal glands just as in the small intestine. The muscularis of the appendix has two layers (inner circular andouter longitudinal) as elsewhere in the alimentary tract.

AETIOLOGY

1. Age and Sex:

No age is immune from the risk of developing appendicitis, which has been reported in new born (Shinaberger JH-1957) and also at the extremes of age. It is rare under the age of four year and after the age of 50 yrs. About 65% of the patients are under the age of 30 yrs and only 2% are 60 yrs and above. The incidence of appendicitis is maximum between

20 to 30yrs[3].

In teenagers and young adults - there is a slight male preponderance of 3:2. While in adults, the incidence of appendicitis is approximately 1.4 times greater in men than in women.

2. Faecaliths:

Non-calcified inspissated faecal masses are a common finding in a large proportion of appendices removed for acute disease. Ulceration or perforation usually occurs at or near a faecaliths may turn diffuse inflammatory lesion into gangrene.

3. Bacterial factors:

Aerobic and Facultative	Anaerobic
Gram-negative **bacilli** *Escherichia* *coli Pseudomonas* *aeruginosa Klebsiella*	**Gram-negative** **bacilli** Other *Bacteroide*s species *Bacteroides fragilis*
Gram-positive cocci *Streptococcus anginosus*	**Gram-positive cocci** *Peptostreptococcus* species
Other *Streptococcu*s species *Enterococcus* species	**Gram-positive bacilli** *Clostridium* species

Table 1. Common Organisms seen in Patients with Acute appendicitis

4. Bands and Adhesions:

Various abnormal peritoneal attachments of congenital origin have been described and if these cause kinking of the appendix, it results into obstruction. Inflammatory or acquired adhesions due to repeated attacks of appendicitis may induce final acute obstructive picture.

5. Strangulation within a hernial Sac:

Strangulation or trauma of the appendix, which lies in an internal or external hernial sac, may induce progressive changes similar to strangulated small bowel. Diffuse inflammation of an appendix in hernial sac may be aggravated by the obstructive effect at the neck of the sac. Amyand removed the first gangrenous appendix from the inguinal hernia[2]. Chatter (1966) removed the inflamed appendix from the femoral hernial sac.

6. Trauma:

This is a very rare cause of acute appendicitis, if the attack of acute appendicitis follows within 24 hrs after a blunt injury to right iliac region the probable cause of appendicitis is due to the displacement of faecaliths by trauma to the abdomen i.e. to the right iliac region and causing sudden obstruction. Birrel (1928) described four cases of this type, while Black (1948) reported 2 cases and Bhaje Kar (1953) 1 case[42].

PATHOGENESIS

Obstruction of the lumen is the dominant etiologic factor in acute appendicitis. Faecaliths are the most common cause of appendicular obstruction. Less common causes are hypertrophy of lymphoid tissue, inspissated barium from previous x-ray studies, tumours, vegetable and fruit seeds, and intestinal parasites. The frequency of obstruction rises with the severity of the inflammatory process. Faecaliths are found in 40% of cases of simple acute appendicitis, in 65% of cases of gangrenous appendicitis without rupture, and in nearly 90% of cases of gangrenous appendicitis with rupture.

The inflammatory process soon involves the serosa of the appendix and in turn parietal peritoneum in the region, which produces the characteristic shift in pain to the right lower quadrant.

The mucosa of the GI tract, including the appendix, is susceptible to impairment of blood supply; thus its integrity is compromised early in the process, which allows bacterial invasion. As progressive distension encroaches on, first the venous return and subsequently the arteriolar inflow, the area with the poorest blood supply suffers most: ellipsoidal infarcts develop in the antimesenteric border. As distension, bacterial invasion, compromise of vascular

supply, and infarction progress, perforation occurs, usually through one of the infarcted areas on the antimesenteric border. Perforation generally occurs just beyond the point of obstruction rather than at the tip because of the effect of diameter on intraluminal tension.

This sequence is not inevitable, however, and some episodes of acute appendicitis apparently subside spontaneously. Many patients who are found to have acute appendicitis at operation give a history of previous similar, but less severe, attacks of right lower quadrant pain. Pathological examination of the appendices removed from these patients often reveals thickening and scarring, suggesting old, healed acute inflammation

The strong association between delay in presentation and appendicular perforation supported the proposition that appendicular perforation is the advanced stage of acute appendicitis; however, recent epidemiologic studies have suggested that non perforated and perforated appendicitis may, in fact, be different diseases.[45]

PATHOLOGY

Morphology

Appendicular inflammation is associated with obstruction in 50% to 80% of cases, usually in the form of a faecalith and, less commonly, a gallstone, tumor, or ball of worms (oxyuriasis vermicularis).

Continued secretion of mucinous fluid in the obstructed viscus presumably leads to a progressive increase in intraluminal pressure sufficient to cause eventual collapse of the draining veins. Ischemic injury then favors bacterial proliferation with additional inflammatory edema and exudation, further embarrassing the blood supply. Nevertheless, a significant minority of inflamed appendices have no demonstrable luminal obstruction, and the pathogenesis of the inflammation remains unknown.

At the earliest stages, only a scanty neutrophilic exudate may be found throughout the mucosa, submucosa, and muscularis propria. Subserosal vessels are congested, and often there is a modest perivascular neutrophilic infiltrate. The inflammatory reaction transforms the normal glistening serosa into a dull, granular, red membrane; this transformation signifies early acute appendicitis for the operating surgeon. At a

later stage, a prominent neutrophilic exudate generates a fibrinopurulent reaction over the serosa.

As the inflammatory process worsens, there is abscess formation within the wall, along with ulcerations and foci of suppurative necrosis in the mucosa. This state constitutes acute suppurative appendicitis.

Further vascular compromise leads to large areas of hemorrhagic green ulceration of the mucosa and green-black gangrenous necrosis through the wall, extending to the serosa, creating acute gangrenous appendicitis, which is quickly followed by rupture and suppurative peritonitis.

The histological criterion for the diagnosis of acute appendicitis is neutrophilic infiltration of the muscularis propria. Usually, neutrophils and ulcerations are also present within the mucosa. Since drainage of an exudate into the appendix from alimentary tract infection may also induce a mucosal neutrophilic infiltrate, evidence of muscular wall inflammation is requisite for the diagnosis.

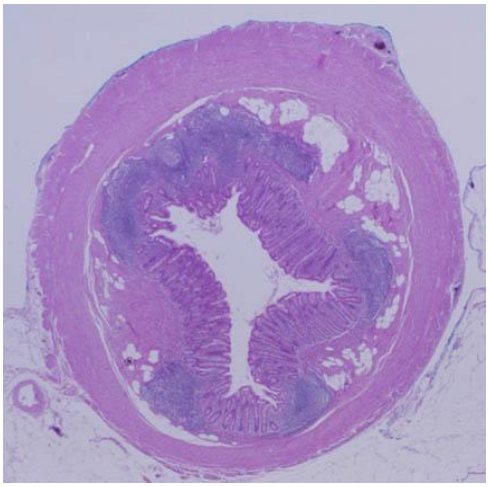


Figure 5: Normal histology of Appendix

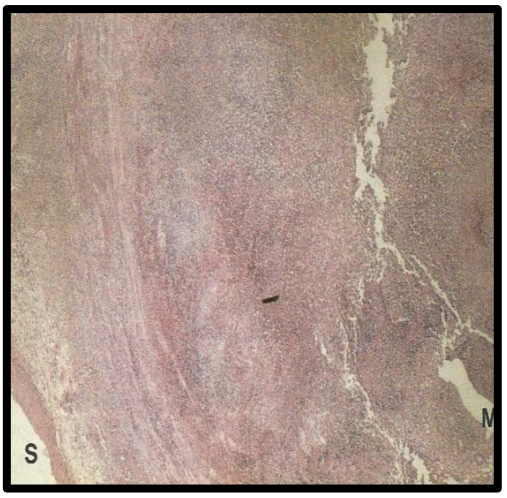


Figure 6. Histology of inflamed Appendix

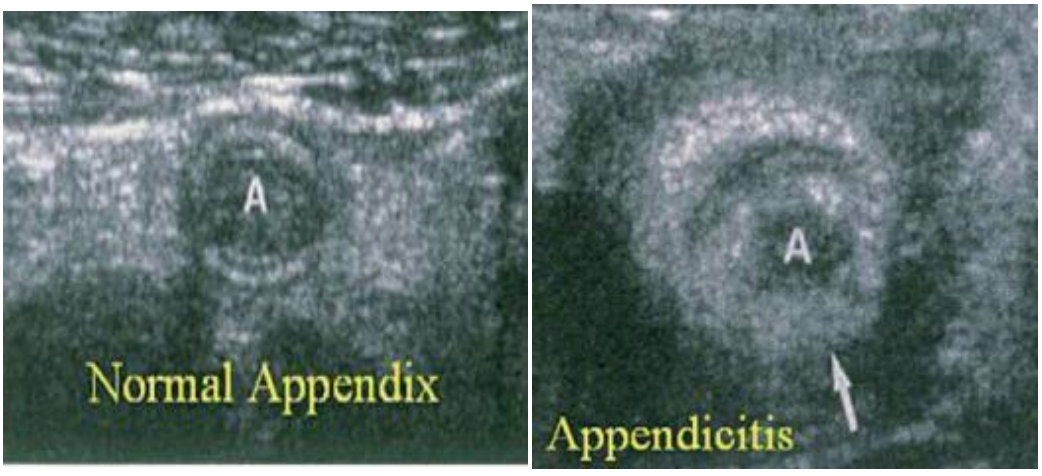


Figure 7. USG finding of a normal appendix and inflammed appendix

DIAGNOSIS

History

The classical features of acute appendicitis begin with poorly localised colicky abdominal pain. This is due to mid-gut visceral discomfort in response to appendicular inflammation and obstruction. The pain is frequently, first, noticed in the peri- umbilical region and is similar to, but less intense than, the colic of small bowel obstruction. Central abdominal pain is associated with anorexia, nausea and usually one or two episodes of vomiting that follow the onset of pain (Murphy" s triad). Most common clinical feature is anorexia. The patient often gives a history of similar discomfort that settled spontaneously. A family history is also useful as up to one-third of children with appendicitis have a first-degree relative with a similar history.

Vomiting*:* Due to reflex pylorospasm.

Physical examination

The diagnosis of appendicitis made usually by the clinical examinations rather than the lab investigations or history.

The charecteristic features low-grade fever, localised RIF tenderness, guarding and rebound tenderness. On Inspection,there may

be decreased abdominal movements during respiration.

On palpation, from the left iliac fossa moving towards the right iliac fossa, one can able to feel muscle guarding in the McBurney" s point. Asking the patient to cough or gentle percussion over the site of maximum tenderness will elicit rebound tenderness.

Cutaneous hyperaesthesia may be demonstrable in the right iliac fossa, but is rarely of diagnostic value.

Multiple signs can be detected on physical examination to contribute to the diagnosis of appendicitis.

1. ***Mc Burney's sign:*** Maximum tenderness at Mc Burney" s point.
2. ***Blumberg's sign:*** A hand kept in the right iliac fossa is progressively pressed with each movement of expiration. It is then removed suddenly; the patient will wince or cry with pain, if the sign is positive, this indicates inflammation of the parietal peritoneum. It is useful sign in the absence of guarding or rigidity.
3. ***The pointing sign:*** The patient have to locate the site of origin of pain and its spread
4. ***Rovsing's sign:*** This sign is positive as a result of pressure

on the left side of the colon, forcing the gas into the caecum distending the caecum and surrounding of the inflamed focus resulting in pain.

5. ***Psoas sign:*** Pain with flexion of the leg at the right hip, can be seen with a retrocecal appendix due to inflammation adjacent to the psoas muscle.

6. ***The Cope's(obturator) sign:*** Pain with rotating the flexed right thigh internally, indicates inflammation adjacent to the obturator muscle in the pelvis.

7. ***Sherren's sign:*** Sherren in 1925, pointed out this Sherren's triangle and is defined as the triangle bounded by lines joining umbilicus, right anterior superior iliac spine and pubic symphysis. Hyperesthesia is elicited by gently striking the skin.

It is compared with left side. If hyperesthesia is present it indicates the perforation of the appendix. This sign is although classic, it is not reliable. It depends upon the discrimination capacity of the patient.

8. ***Baldwin's test for retrocaecal appendix****:* After identifying the tender spot in the right flank, light pressure is maintained over the spot and the patient is asked to lift the right lower limb keeping the knee in straight position. This produces increased pain in the loin and the patient drops the leg with pain. This is a positive sign of retrocaecal appendicitis. Sometimes there may be irritation of the ureters with pain shooting around flank. Sometimes red blood corpuscle may be found in the urine.

9. ***Shifting Tenderness (Alder's):*** The most tender spot is marked first, the patient is put in left lateral position and point of maximum tenderness is marked again. If the tender spot shifts probably it is not a case of appendicitis. This sign is useful to differentiate appendicitis from mesenteric lymphadenitis and painful uterine conditions in pregnancy.

INVESTIGATIONS

Laboratory Tests

There is no gold standard test for appendicitis but it may be helpful in arriving the diagnosis.

WBC

A White Blood Cel count (WBC)may have significant role with leucocytosis, with more than 75% neutrophils.

A completely normal leukocyte count and differential count is found in about 10% of patients with acute appendicitis. A high white blood cell count (>20,000/mL) suggests complicated appendicitis with either gangrene or perforation.

In early cases WBC count may be normal.There may be raise in WBC count over the time.

C-reactive protein

C-reactive protein (CRP) is an acute-phase reactant synthesized by the liver in response to infection or inflammation and rapidly increases within the first 12 hours. CRP has been reported to be useful in the diagnosis of appendicitis; however, it lacks

specificity and cannot be used to distinguish between sites of infection. CRP levels of greater than 1 mg/dl are commonly reported in patients with appendicitis, but very high levels of CRP in patients with appendicitis indicate gangrenous evolution of the disease, especially if it is associated with leukocytosis and neutrophilia.

Imaging Studies

The various imaging techniques for diagnosis include plain Xray, USG and CT scan..

Plain radiographs

Plain X-ray may show lumbar scoliosis towards right due to psoas spasm which is not uncommon; faecolith on the right side; obliteration of preperitoneal fat line due to retrocaecal appendicitis; segmental ileus in caecum and terminal ileum; speckled extraluminal gas in right iliac fossa, gas in appendix, pneumoperitoneum (very rare); intestinal obstruction (occasionally only); soft tissue mass in mass or abscess of appendix—all these features are very much nonspecifi c. X-ray is useful to rule out DU perforation, intestinal obstruction, ureteric stone.

Radio-opaque appendix in a plain X-ray. It could be calcified or have calcified content.

Ultrasonography (USG)

Sonographic criterias for appendicitis (85% Specifi city)

Noncompressible appendix of size > 6 mm AP diameter, hyperechoic thickened appendix wall > 2 mm—*target sign*. Appendicolith.

Interruption of submucosal continuity.

Periappendicular fluid.

Ultrasonography has the advantages of being a non-invasive modality requiring no patient preparation that also avoids exposure to ionizing radiation. For these reasons, it is commonly used in children and in pregnant women with doubtful diagnosis.

Pelvic ultrasound can be especially useful in excluding pelvic pathology, such as tubo-ovarian abscess or ovarian torsion, which may mimic acute appendicitis.

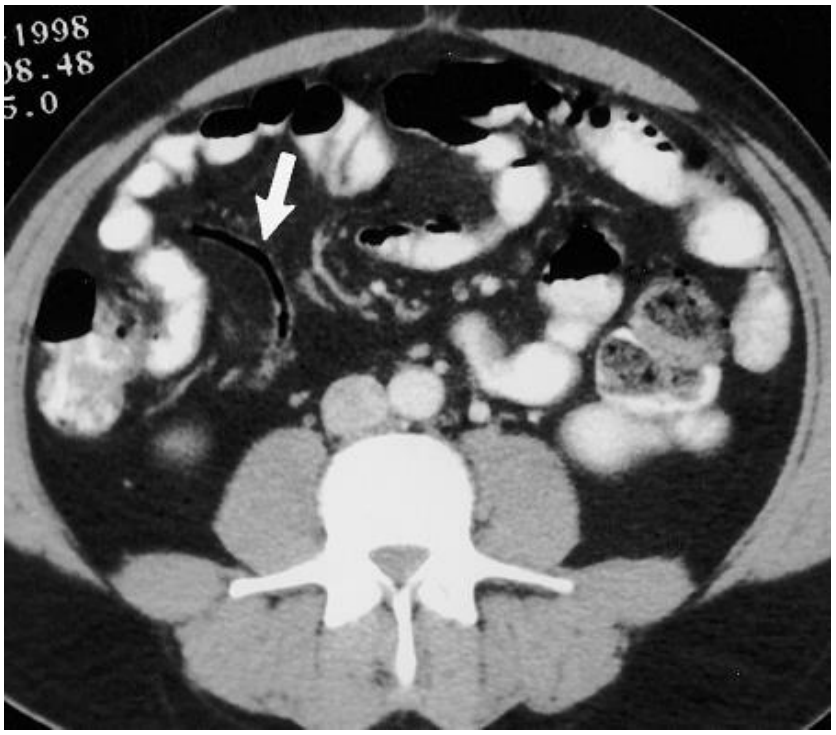
Computed tomography

Computed tomography (CT) is commonly used in the evaluation of adult patients with suspected acute appendicitis, especially so in the elderly.[3] CT has a high sensitivity and specificity in the diagnosis of appendicitis,52 and rule out other causes of abdominal pain that mimic appendicitis.

In general, CT findings of appendicitis increase with the severity of the disease. Classic findings include a distended appendix greater than seven mm in diameter and circumferential wall thickening, which may give the appearance of a halo or target. As inflammation progresses, one may see periappendicular fat stranding, edema, peritoneal fluid, phlegmon, or a periappendicular abscess.

Spiral Computed Tomography

The use of spiral computed tomography in patients with equivocal clinical presentation suspectred of having acute appendicitis led to a significant improvement in the preoperative diagnosis and a lower negative appendectomy rate. Appendiceal computed tomography is an accurate technique even if performed in the daily routine of scanning.



Contrast enhanced spiral CT showing inflamed appendix

Diagnostic Laparoscopy

Although most patients with appendicitis will be accurately diagnosed based on history, physical exam, laboratory studies, and if necessary, imaging techniques, there are a small number in whom the diagnosis remains elusive. For these patients, diagnostic laparoscopy can provide both a direct examination of the appendix and a survey of the abdominal cavity for other possible causes of pain.

Laparoscopy can serve as both a diagnostic and therapeutic maneuver for patients with acute abdominal pain and suspected acute appendicitis.

Laparoscopy is probably most useful in the evaluation of females with lower abdominal complaints, because appendicectomy is performed on a normal appendix in as many as 30 to 40% of these patients.

Scoring Systems

A number of clinical and laboratory-based scoring systems have been devised to assist diagnosis. The most widely used is the Alvarado score. A score of seven or more is strongly predictive of acute appendicitis.

Features	Score
Symptoms	
Migratory RIF pain	1
Anorexia	1
Nausea and vomiting	1
Signs	
Tenderness (RIF)	2
Rebound tenderness	1
Elevated temperature	1
Laboratory	2
Leucocytosis	
Shift to left	1

Table 2: The Alvarado score

Liver Function Tests

Importance of hyperbilirubinemia or elevated Serum Bilirubin (serum bilirubin) and its association in acute appendicitis has being postulated recently. It is hypothesized that an association exists between hyperbilirubinemia and acute appenditics and its complications such as appendicular perforation.[55]

BILIRUBIN METABOLISM

Bilirubin is produced from the destruction of senescent RBC's by the removal of the iron by the action of the enzyme heme oxygenase; the reaction liberates carbon monoxide, the only reaction in the body releasing carbon monoxide. The intermediate product being biliverdin. Bilirubin a water insoluble compound is transported to the liver bound to albumin.

In the liver the bilirubin is taken up activity by two mechanisms. The first being a membrane bound carrier protein and the second being by two cytoplasmic proteins namely protein Y and Z. These proteins pick up the bilirubin diffusing into the cytoplasm.

Once in the hepatocyte the bilirubin is bound to glucuronic acid thus forming bilirubin mono and diglucuronide by the enzyme UDP glucuronyl transferase. The enzyme reduced products get excreted as stercobilinogen.

The kidneys excrete a part of the absorbed bilirubin as urobilinogen and the rest enters the enterohepatic circulation.

Hyperbilirubinemia and appendicitis

Hyperbilirubinemia, has not been considered as a potential marker for preoperative diagnosis of acute appendicitis and appendicular perforation until now.Increased secretion and decreased bilirubin clearance has a role in the hyperbilirubinemia of patients with appendicular perforation.

Bacterial infections cause hepatic dysfunction leading to abnormalities in bile acid production and bile flow. This results in hyperbilirubinemia.

Extrahepatic bacterial infection, as in perforated appendicitis, have a proinflammatory cytokine and nitric oxide – triggered cholestasis by affecting hepatocellular and bile duct function.[60]

Most common bacterial species causing acute appendicitis are *Escherichia coli* and *Bacteroides fragilis.* These organisms interfere with hepatocyte microcirculation and cause sinusoidal damage.

E. Coli endotoxin leads to impaired bile production.And also, *E. Coli* infection causes hemolysis of erythrocytes. This leads to hyperbilirubinemia.

Cholestasis in severe bacterial infection, particularly in childhood or post operatively, is presumably hepatocellular in nature. It can also be related to cholestatic effect of endotoxin on sodium-potassium-ATPase.

All the constituents of bile show an increased level in serum. Conjugation of biliary substance is intact but excretion is defective. Serum alkaline phosphatase is raised. The rise is due to increased synthesis or release of enzymes from liver or biliary plasma membrane.

The minimal hepatocellular damage may be suspected by noting minimal elevated transaminase value and sometimes serum bilirubin.

There are no sufficient number of studies involving large number of patients to ascertain relationship between hyperbilirubinemia and acute appendicitis.

MATERIALS AND METHODS

The study was conducted in the Department of General Surgery, Govt.Rajaji Hospital and Medical College, Madurai during the period of August 2017 to August 2018.

Study design

A prospective non randomised study.

Source

The present study was conducted in the Department of Surgery, Govt.Rajaji Hospital and Medical College, Madurai

Study period

One year from August 2017 to August 2018..

Source of data

Patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation under the Department of Surgery, Govt.Rajaji Hospital and Medical College, Madurai during the study period.

Sample size

A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation were studied.

Sampling method

The sample size was calculated based on the following formula.

$$n = \frac{Z^2 \times p \times q}{d^2}$$

Where,

n = Sample size

Z = 1.96 ≈ 2 (considering confidence as 95%)

p = prevalence (prevalence is taken as 50% as exact prevalence is not known)

q = 100 – p that is, 50%

d = Absolute error which was 10%

Selection criteria

Inclusion

- All patients diagnosed as acute appendicitis clinically on admission.
- All patients diagnosed as appendicular perforation clinically on admission.

- For both these groups, only patients with histopathological report suggestive of acute appendicitis or appendicular perforation were included.

Exclusion

- All patients documented to have a past history of-
  - Jaundice or Liver disease.
  - Chronic alcoholism (that is intake of alcohol of > 40 g/day for Men and > 20 g/day in Women for 10 years).[71]
  - Hemolytic disease.
  - Acquired or congenital biliary disease.
- All patients with positive HBsAg.
- All patients with cholelithiasis.
- All patients with cancer of hepato-biliary system.

Procedure

Ethical clearance has been obtained from "Ethical Clearance Committee" of the institution for the study. Based on the selection criteria patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation under Department of Surgery, Govt.Rajaji Hospital and medical college,Madurai during the study period werescreened. The nature of the study was explained to the patients.

The patients were included in this study after getting written informed consent. History and clinical examination was done for all and recorded in the profoma

The following tests were carried out on admission.

- Routine blood investigations (Complete blood count, platelet count, reticulocyte count).
- Peripheral smear to rule out hemolytic anemia.
- Serum haptoglobulin if peripheral smear and blood tests indicate features of hemolytic anemia.
- Serum Bilirubin (Total and Direct bilirubin).
- Liver Function Tests (LFTs) which include;
    - SGPT (Alanine transaminase).
    - SGOT (Aspartate transaminase).
    - ALP (Alkaline phosphatase).
- Seropositivity for HbsAg
- Urine analysis (routine and microscopy).

The serum bilirubin and LFTs were carried out using the Auto Analyser machine available in the hospital and HbsAg was tested by ELISA / Spot technique using HEPALISA or HEPACARD kit.

Reference Range of Serum Bilirubin and Liver Enzymes[23]

Test	Normal Range
Serum Bilirubin	
Total	0.3 - 1.0 mg/dl
Direct	0.1 – 0.3 mg/dl
Liver Enzymes	
SGPT	0 – 35 U/L
SGOT	0 – 35U/L
ALP	30 – 120U/L

The results were grouped as Normal or Raised (hyperbilirubinemia) as per the above reference values.

Statistical analysis

The data obtained was tabulated on Microsoft excel spreadsheet and analysed as below.

- Patients with clinical diagnosis of acute appendicitis having hyperbilirubinemia were expressed in percentage as

$$= \frac{\text{Patients with clinical diagnosis of acute appendicitis with elevated Serum bilirubin level}}{\text{All patients with clinical diagnosis of acute appendicitis}}$$

- Mean of the level of elevation of Serum bilirubin was calculated for patients with clinical diagnosis of acute appendicitis.

- Patients with clinical diagnosis of appendicular perforation having hyperbilirubinemia were expressed in percentage as;

$$= \frac{\text{Patients with clinical diagnosis of appendicular perforation with elevated Serum bilirubin}}{\text{All patients with clinical diagnosis of appendicular perforation}}$$

- Mean of the level of elevation of serum bilirubin were calculated for patients with clinical diagnosis of appendicular perforation.

- A hypothesis was made based on the observation of the level of the two means.

- Also, sensitivity, specificity, positive predictive value, negative predictive value and Odds ratio was determined by 2 x 2 table as below.

	Acute appendicitis	Appendicular perforation
Raised Sr. Bilirubin	A	B
Normal Sr. Bilirubin	C	D
	a + c	b + d

Sensitivity: $\frac{a}{a+c} \times 100$

Specificity: $\frac{d}{b+d} \times 100$

Positive predictive value : $\frac{a}{a+b} \times 100$

Negative predictive value: $\frac{d}{c+d} \times 100$

Odds ratio: $\frac{ad}{bc}$

RESULTS

A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation admitted in the Department of General surgery, Govt.Rajaji Hospital and medical college,Madurai were studied.

As per the study, the age group 11-20years is most commonly affected (44%) followed by age group 21-30 (32%). The youngest patients of this study were of 8 years old while the oldest patient was a 70 year lady

Table 3: Distribution of patients by age

Age Group (years)						
≤10	11-20	21-30	31-40	41-50	51-60	61-70
8	44	32	8	3	4	1

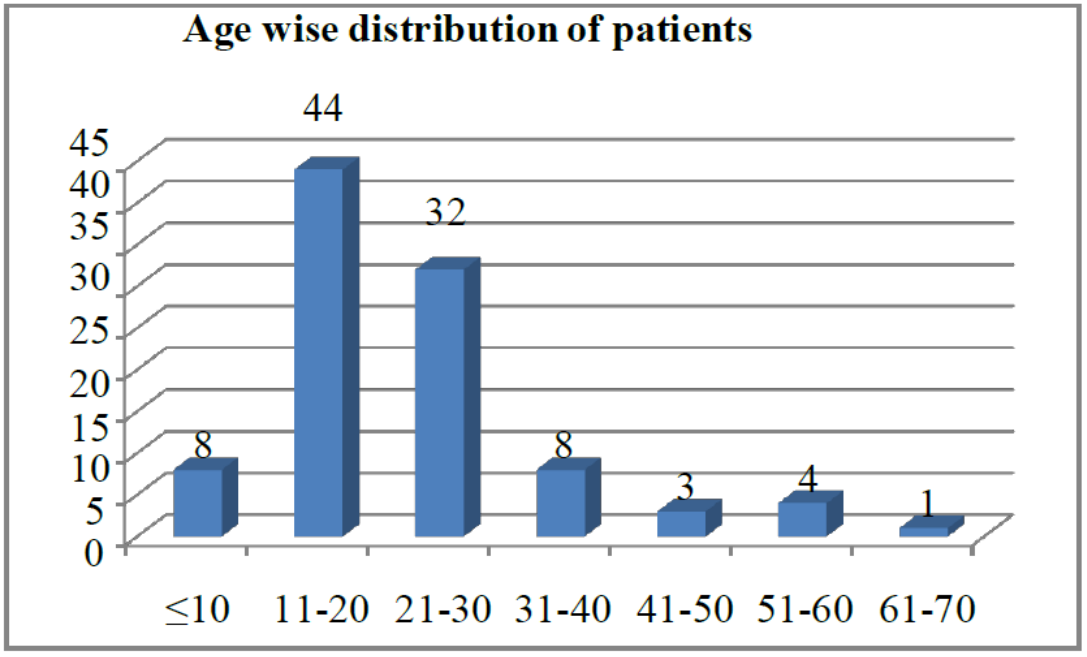

Age wise distribution of patients
45
40
35
30
25
20
15
10
5
0
44
32
8
8
3
4
1
≤10
11-20
21-30
31-40
41-50
51-60
61-70

Table 4: Liver Function Tests

Parameters	Mean	SD
Total bilirubin (mg/dL)	1.5	0.8
Direct bilirubin (mg/dL)	1.0	0.7
Indirect bilirubin (mg/dL)	0.5	0.2
SGOT (U/L)	27.9	12.2
SGPT (U/L)	25.9	11.0
ALP (U/L)	80.8	21.6

The mean Total bilirubin of all 100 patients was 1.5 ± 0.8 mg/dL (range, 0.7 – 2.3 mg/dL) while the Direct bilirubin was 1.0 ± 0.7 mg/dL (range, 0.3-1.7 mg/dL). The mean SGOT and SGPT were 27.9 ± 12.2 U/L (range, 15.7-40.1 U/L) and 25.9 ± 11.0 U/L (range, 14.9 – 35.9 U/L). The mean ALP values were 80.8 ± 21.6 U/L (range, 59.2 -102.4 /L).

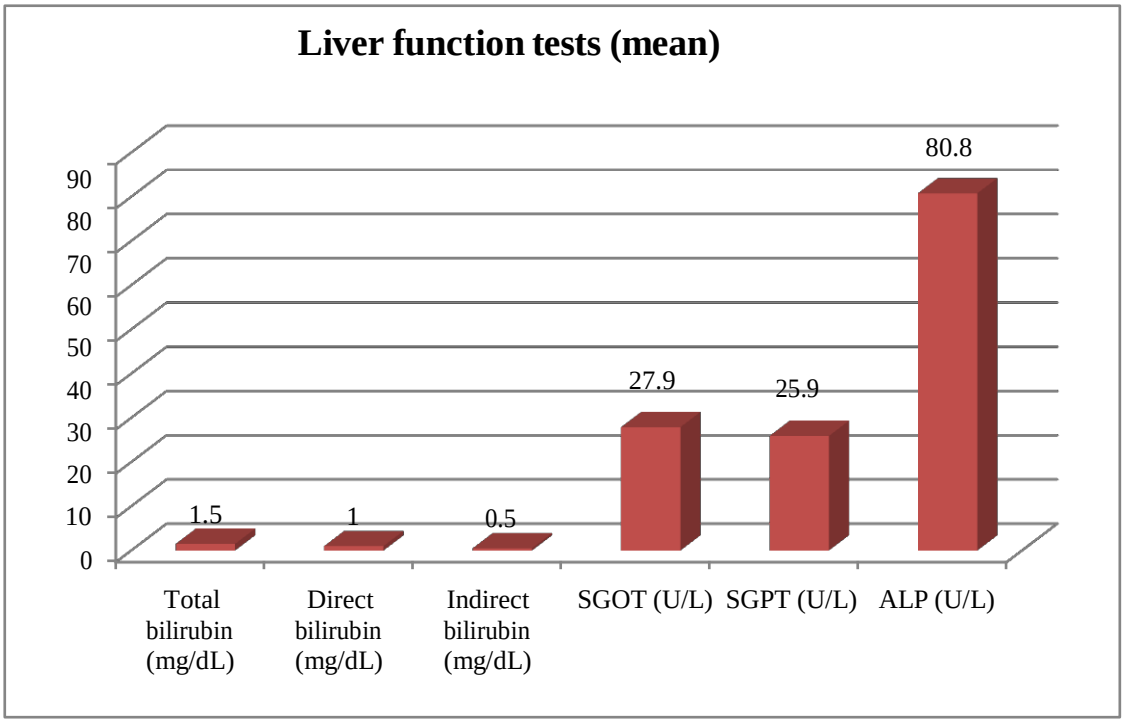

Liver function tests (mean)
90
80
70
60
50
40
30
20
10
0
1.5
1
0.5
27.9
25.9
80.8
Total bilirubin (mg/dL)
Direct bilirubin (mg/dL)
Indirect bilirubin (mg/dL)
SGOT (U/L)
SGPT (U/L)
ALP (U/L)

Table 5: Total bilirubin levels

Total bilirubin (mg/dL)	Number	Percentage
< 1.0	26	26.0
≥ 1.0	74	74.0
Total	**100**	**100.00**

26 patients (26%) of all 100 patients were found to have normal bilirubin levels (≤ 1.0 mg/dL), while 74 patients (74%) had raised bilirubin levels (> 1.0 mg/dL).

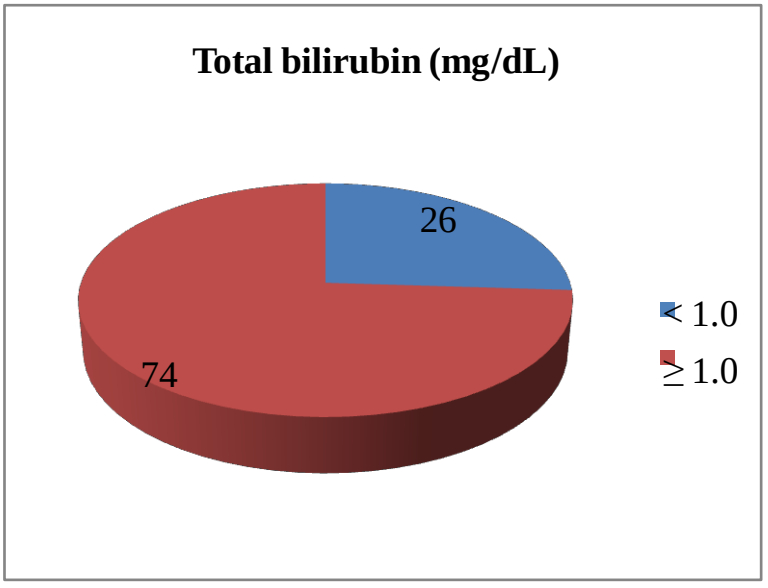


Table 6: Bilirubin levels in patients with uncomplicated acute appendicitis as diagnosis

Total bilirubin (mg/dL)	Distribution in Patients with uncomplicated Acute Appendicitis	
	Number	Percentage
> 1.0	58	71.60
≤ 1.0	23	28.40
Total	**81**	**100.00**

Of 81 patients diagnosed as uncomplicated acute appendicitis, 58 patients (71.6%) had raised bilirubin levels (> 1.0 mg/dL), while the remaining 23 patients (28.4%) had normal levels (≤ 1.0 mg/dL).

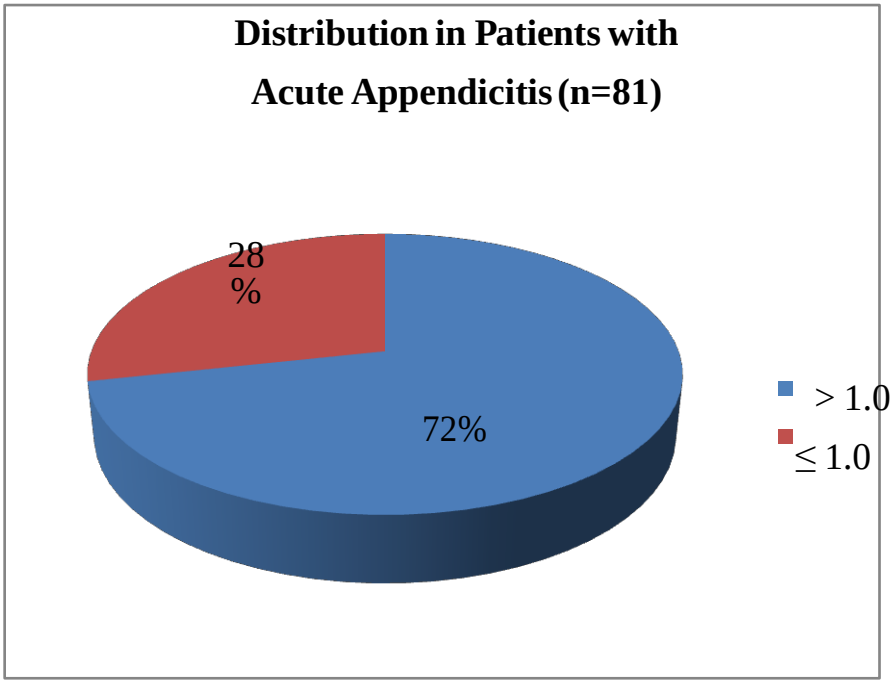


Table 7. Bilirubin levels in patients with Appendicular perforation diagnosis

Total bilirubin (mg/dL)	Distribution in Patients with Appendicular perforation	
	Number	Percentage
> 1.0	16	84.21
< 1.0	03	15.79
Total	**19**	**100.00**

19 patients diagnosed as Appendicular perforation, 16 patients (84.21%) had raised bilirubin levels (> 1.0 mg/dL), while the remaining 03 patients (15.79%) had normal levels (≤ 1.0 mg/dL).

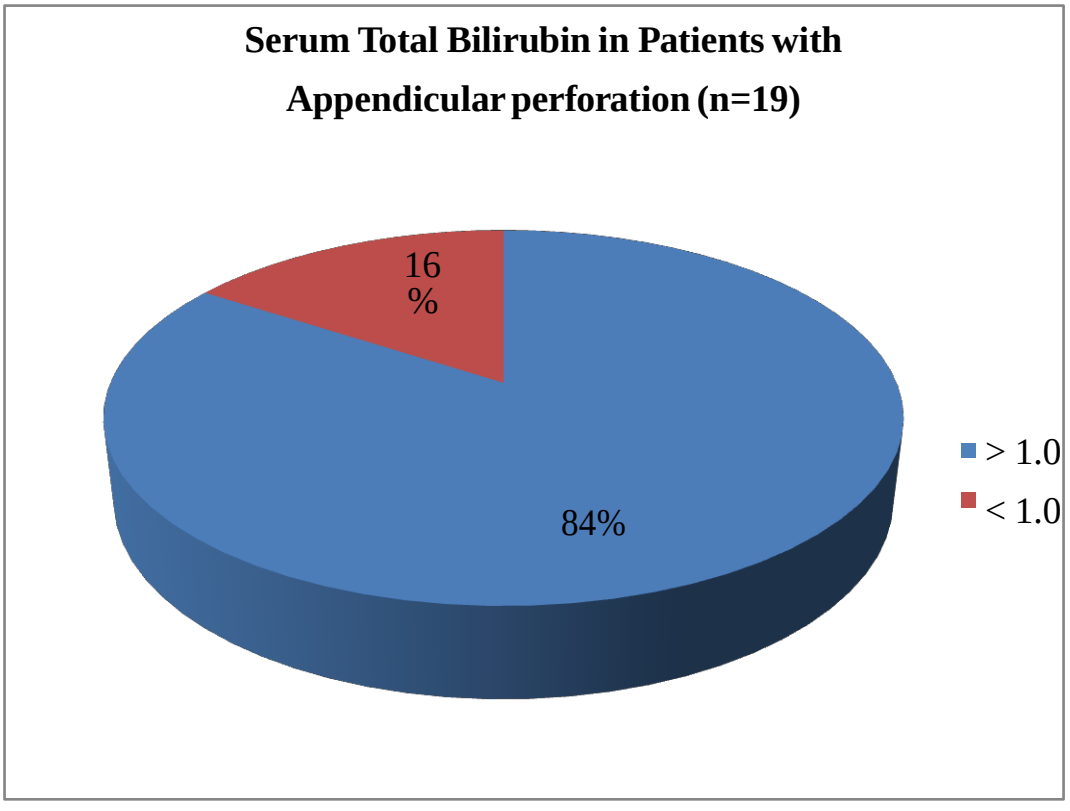


Table 8. Histopathological diagnosis

Diagnosis	Distribution (n=100)	
	Number	Percentage
Acute appendicitis	81	81
Appendicular perforation	19	19
Total	**100**	**100**

Histopathologically, 81 patients (81%) were confirmed as Acute appendicitis while 19 patients (19%) were diagnosed with Appendicular perforation.

Histopathological diagnosis

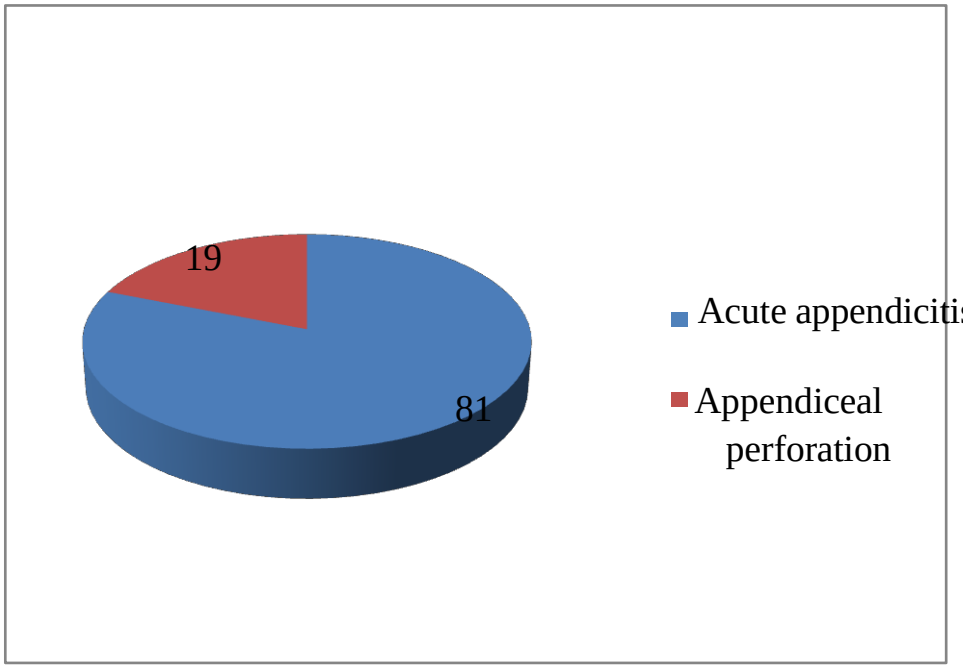


Table 9. Comparison of mean serum bilirubin levels in patients with acute appendicitis and Appendicular perforation

Bilirubin levels (mg/dL)	Diagnosis			
	Acute appendicitis		Appendicular perforation	
	Mean	SD	Mean	SD
Total bilirubin	1.4	0.65	1.9	1.16
Direct bilirubin	0.9	0.57	1.2	1.06
Indirect bilirubin	0.5	0.21	0.70	0.33

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.4 ±0.65 mg/dL (range, 0.75 – 2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.9±1.16 mg/dL (range, 0.74 – 3.06 mg/dL). The Direct bilirubin and Indirect bilirubin in patients diagnosed with Acute appendicitis were 0.9±0.57 mg/dL and 0.5±0.21 respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with Appendicular perforation were 1.2±1.06 mg/dL and 0.70±0.33 mg/dL respectively.

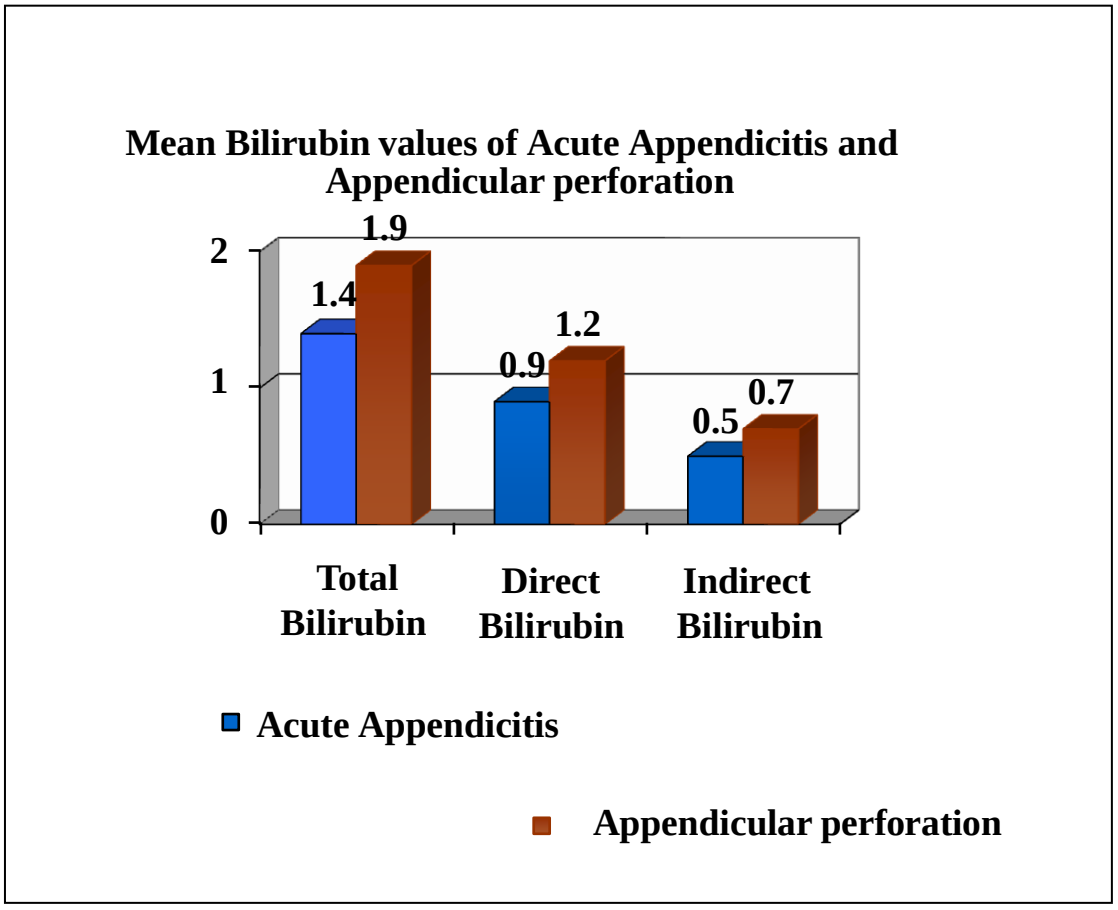

Mean Bilirubin values of Acute Appendicitis and Appendicular perforation
2
1
0
1.4
1.9
0.9
1.2
0.5
0.7
Total Bilirubin
Direct Bilirubin
Indirect Bilirubin
Acute Appendicitis
Appendicular perforation

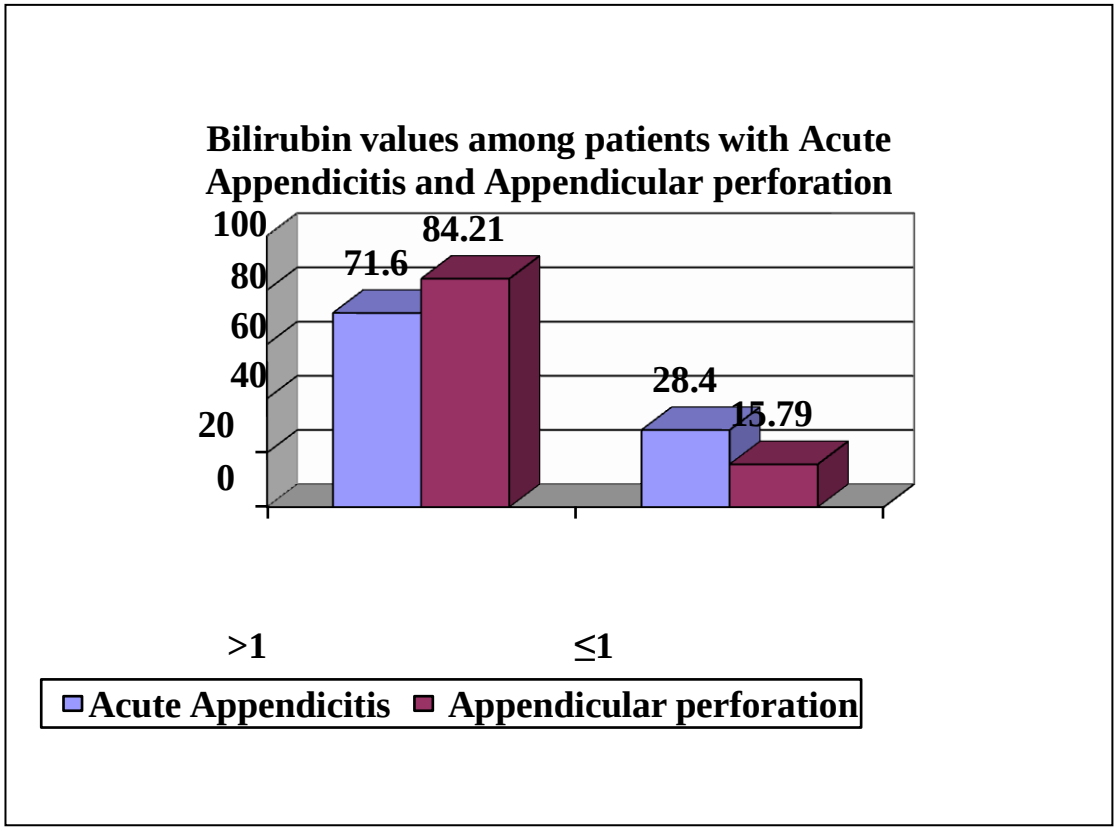
Table 10. Correlation of acute appendicitis and Appendicular perforation with total serum bilirubin levels

Serum bilirubin (mg/dL)	Final diagnosis (n=100)			
	Acute appendicitis (n=81		Appendicular perforation (n=19)	
	Number	%	Number	%
> 1.0	58	71.6	16	84.21
≤ 1.0	23	28.4	03	15.79
Total	**81**	**100.00**	**19**	**100.00**

58 patients (71.6%) of the total patients diagnosed with Acute appendicitis (n=81) were found to have elevated bilirubin levels (> 1.0 mg/dL) while 23 patients (28.4%) had normal bilirubin levels (≤ 1.0 mg/dL). Similarly,

16 patients (84.21%) of the total patients diagnosed with Appendicular perforation (n=19) were found to have elevated bilirubin levels (> 1.0 mg/dL)

while 03 patients (15.79%) had normal bilirubin levels (≤ 1.0 mg/dL).


Bilirubin values among patients with Acute Appendicitis and Appendicular perforation
100
80
60
40
20
0
71.6
84.21
28.4
15.79
>1
≤1
Acute Appendicitis
Appendicular perforation

From Table, following values were calculated as -

Sensitivity

$$= \frac{a}{a + c} = \frac{58}{58 + 16} = 71.6\%$$

Therefore, sensitivity of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 71.6%.

Specificity

$$= \frac{d}{b + d} = \frac{3}{16 + 3} = 15.79\%$$

Therefore, specificity of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 15.79%

Positive predictive value

$$= \frac{a}{a + b} = \frac{58}{58 + 16} = 78.38\%$$

Therefore, Positive predictive value of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 78.38%.

Negative predictive value

$$= \frac{d}{c + d} = \frac{3}{23 + 3} = 11.54\%$$

Therefore, Negative predictive value of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 11.54%.

Odds ratio:

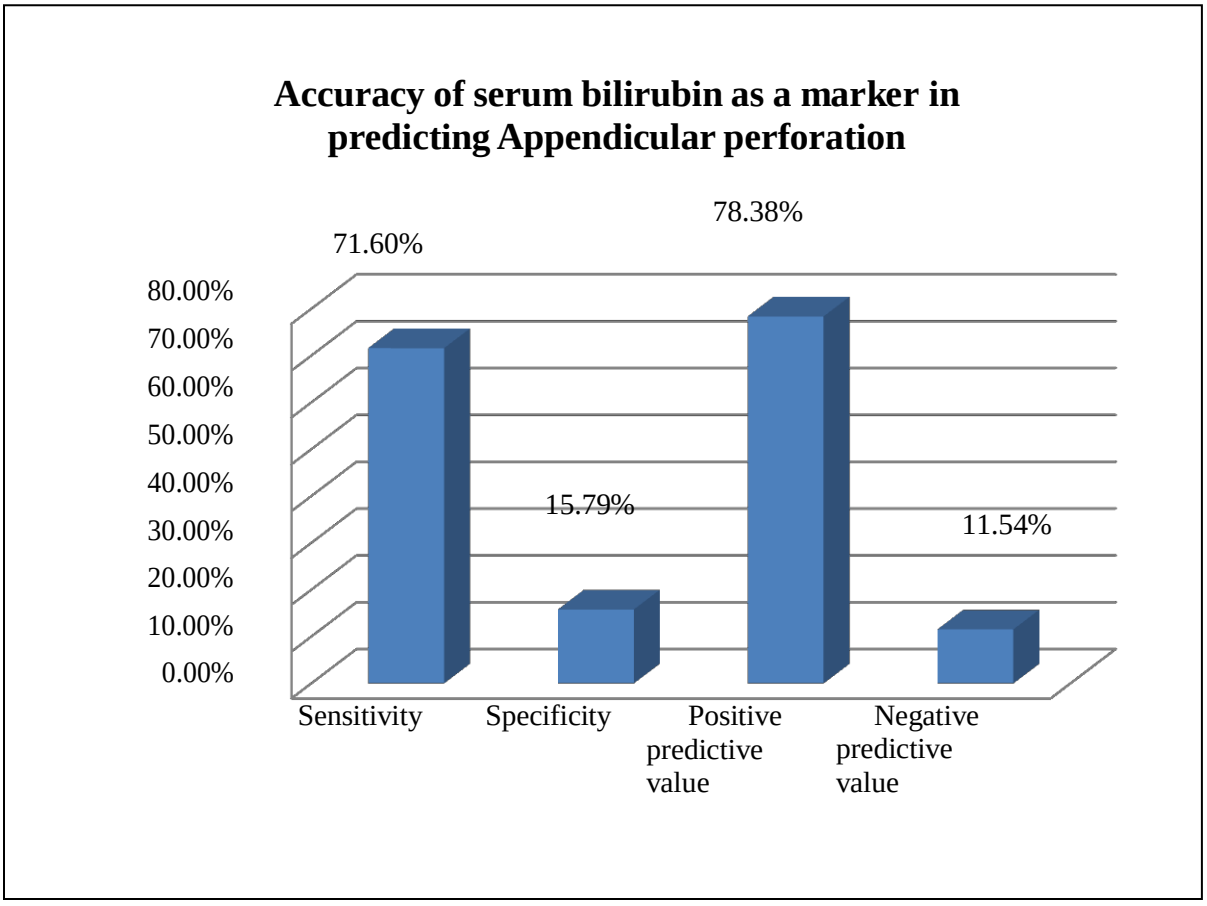
$$= \frac{ad}{bc} = \frac{58 \times 3}{23 \times 16} = 0.472$$

Therefore, Odds ratio is 0.472.

Table 11. Accuracy of serum bilirubin as a marker in predicting Appendicular perforation

	Accuracy
Sensitivity	71.6%
Specificity	15.79%
Positive predictive value	78.38%
Negative predictive value	11.54%
Odds ratio	0.472

The Sensitivity and Specificity of serum bilirubin as a marker in predicting acute appendicitis and Appendicular perforation was 71.6% and 15.79% respectively. Similarly the Positive predicative value and Negative predicative value for the same is 78.38% and 11.54% respectively. The Odds r atio was calculated to be 0.472.


Accuracy of serum bilirubin as a marker in predicting Appendicular perforation
71.60%
15.79%
78.38%
11.54%
80.00%
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
Sensitivity
Specificity
Positive predictive value
Negative predictive value

DISCUSSION

Acute appendicitis is the most common cause of " acute abdomen " in young adults. Appendicectomy is the most frequently performed emergency abdominal operation and is often the first major procedure performed by a surgeon in training.[1] About 8% of people in Western countries have appendicitis at some time in their lifetime.[3]

The peak incidence of acute appendicitis is in the second and third decade of life. It is relatively rare in infants, and becomes increasingly common in childhood and early adult life. The incidence of appendicitis is equal in males and females before puberty. In teenagers and young adults, the male – female ratio increases to 3:2 at age 25.[1] The lifetime rate of appendicectomy is 12% for men and 25% for women, with approximately 7% of all people undergoing appendectomy for acute appendicitis during their lifetime.[33,34]

Obstruction of the lumen is believed to be the major cause of acute appendicitis.[3] Faecoliths are the usual cause of obstruction. Less- common causes are hypertrophy of lymphoid tissue, tumors, intestinal parasites.[23] The bacteriology of normal appendix is similar to that of normal colon.

The principal organism seen in normal appendix, in acute appendicitis, and in perforated appendicitis are *Escherichia Coli* and *Bacteroids fragilis*. However a wide variety of both facultative and anaerobic bacteria may be present.[23]

The diagnosis of acute appendicitis is essentially clinical; however, a decision to operate based on clinical suspicion alone can lead to the removal of a normal appendix in 15 to 50% of cases.[4] The premise that it is better to remove a normal appendix than to delay diagnosis does not stand up to close scrutiny, particularly in the elderly[1] as such procedures are associated with complications in 50% cases.[5] Hence, the diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations.

A new tool to help in the diagnosis of acute appendicitis would thus be welcome.

Serum Bilirubin level elevation will help in the accuracy of clinical diagnosis of acute appendicitis and more importantly help in foreseeing and preventing impeding complications of acute appendicitis.

This study was taken up with this thought – that is it possible to add serum bilirubin as a new laboratory marker to aid in the diagnosis of acute appendicitis and if so, does it have the credibility to help us foresee an impending complication of acute appendicitis?

Importance of hyperbilirubinemia and its association in acute appendicitis has being postulated recently. There are only a few case reports in the available literature that describe the finding of hyperbilirubinemia in patients of acute appendicitis.[54] It is hypothesized that an association exists between hyperbilirubinemia and acute appendicitis and its complications.[54]

The present study was undertaken to study the relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

This study was conducted in the Department of General Surgery, GRH & MMC,Madurai over a period of one

year from August 2017 to August 2018 on 100 patients with clinical diagnosis of Acute appendicitis and Appendicular perforation.

In the present study of the 100 patients enrolled for the study, 56 patients (56%) were males while the remaining 44 patients (44%) were females.The mean age in our study population (100 patients) was 23.1 ± 11.99 years (range, 11.11–35.09 years). This is consistent with the quoted incidence of Appendicitis in the literature where it is most frequently seen in patients in their second through fourth decades of life.[33,34] The average age group in males 24 ± 11.93 years (range, 12.07 –35.93 years) was slightly higher than females 23.1 ± 11.93 years (range, 11.17 –35.03 years).

Hyperbilirubinemia (> 1.0 mg/dL) in our study was found in 74 patients (74%) of all the 100 patients (n=100) enrolled in the study, while 26 patients (26%) had normal bilirubin levels (≤ 1.0 mg/dL). Estrada et al[54] had found hyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.

The mean total serum bilirubin of all 100 patients was 1.5 ± 0.8 mg/dL (range, 0.7 – 2.3 mg/dL), which was above the normal range (≤ 1.0 mg/dL) considered for the study, hence indicating the occurrence

of hyperbilirubinemia. The mean of Direct bilirubin was 1.0 ± 0.7 mg/dL (range, 0.3-1.7 mg/dL) while that of Indirect bilirubin was 0.5±0.2 mg/dL (range, 0.3 – 0.7 mg/dL). Our finding was consistent with hyperbilirubinemia found in a study conducted by Khan S,[15] who found average level of serum bilirubin in his study population to be 2.38 mg/dL.

All patients were found to have SGOT and SGPT within the normal range, thus excluding any associated liver pathology (Exclusion criteria). The mean SGOT and SGPT were 27.9 ± 12.2 U/L (range, 15.7-40.1 U/L) and 25.9 ± 11.0 U/L (range, 14.9 – 35.9 U/L). The mean ALP values were 80.8 ± 21.6 U/L (range, 59.2 -102.4 U/L).

In our study population of 100 patients, 91 patients (91%) were diagnosed as acute appendicitis pre-operatively while 09 patients (9%) were diagnosed with Appendicular perforation.

The diagnosis was confirmed post-operatively by histopathological reports (HPR) and those differing from the pre-operative diagnosis were excluded from the study.

Amongst the patients diagnosed with Acute appendicitis without perforation (n=81), 58 patients (71.6%) were found to have elevated bilirubin (>1.0 mg/dL) while only 23 patients (28.4%) had normal bilirubin levels (≤1.0 mg/dL). In patients diagnosed with Appendicular perforation (n=19), 16 patients (84.21%) had bilirubin elevated (>1.0 mg/dL), while only 3 patients (15.79%) had normal levels (>1.0 mg/dL). Thus, Hyperbilirubinemia was found in most of the patients diagnosed with acute appendicitis (71.6%) or Appendicular perforation (84.21%).

The total leukocyte count was found elevated in just 35 patients (35%) of the total 100 patients. The mean of TLC count in all patients was 10030±3712/mm3 (range, 6318 - 13742/mm3), in which the highest percentage constituted Neutrophils with 71.7% followed by 23.7% by Lymphocytes.

On Ultrasonography, 69 patients (69%) were diagnosed as Acute appendicitis, 13 pateints (13%) as Appendicular perforation and 18 patients (18%) were reported as normal ultrasonographic findings. Ultrasonography per- se was 82% sensitive for appendicitis and/or Appendicular perforation, hence Ultrasonography is a helpful tool in diagnosing appendicitis or perforation.

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.4 ±0.65 mg/dL (range, 0.75 – 2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.9±1.16 mg/dL (range, 0.74 – 3.06 mg/dL). Hence, we see that patients with Appendicular perforation had higher levels of bilirubin as compared to that of acute appendicitis. So we infer that, patients with features suggestive of appendicitis with higher values of bilirubin, are more susceptible of having Appendicular perforation than those with normal or slightly elevated total serum bilirubin.

Sand et al[68] in his study found the mean bilirubin levels in patients with Appendicular perforation to be significantly higher than those with a non- perforated appendicitis.

The Direct bilirubin and indirect bilirubin in patients diagnosed with acute appendicitis were 0.9±0.57 mg/dL and 0.5±0.21 respectively. Similarly, direct bilirubin and indirect bilirubin in patients diagnosed with Appendicular perforation were 1.2±1.06 mg/dL and 0.70±0.33 mg/dL respectively.

The Sensitivity, Specificity, Positive predictive value, Negative predictive value and Odds ratio was calculated from a 2x2 table. Sensitivity and Specificity of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 71.6% and 15.79% respectively. Similarly Positive predictive value and Negative predicative value of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 78.38% and 11.54% respectively. The Odd" s ratio was calculated to be 0.472.

The sensitivity in our study was more than that by Sand et al[68] in which, he found the sensitivity and specificity in his study of hyperbilirubinemia for predicting Appendicular perforation to be 70% and 86.0% respectively.

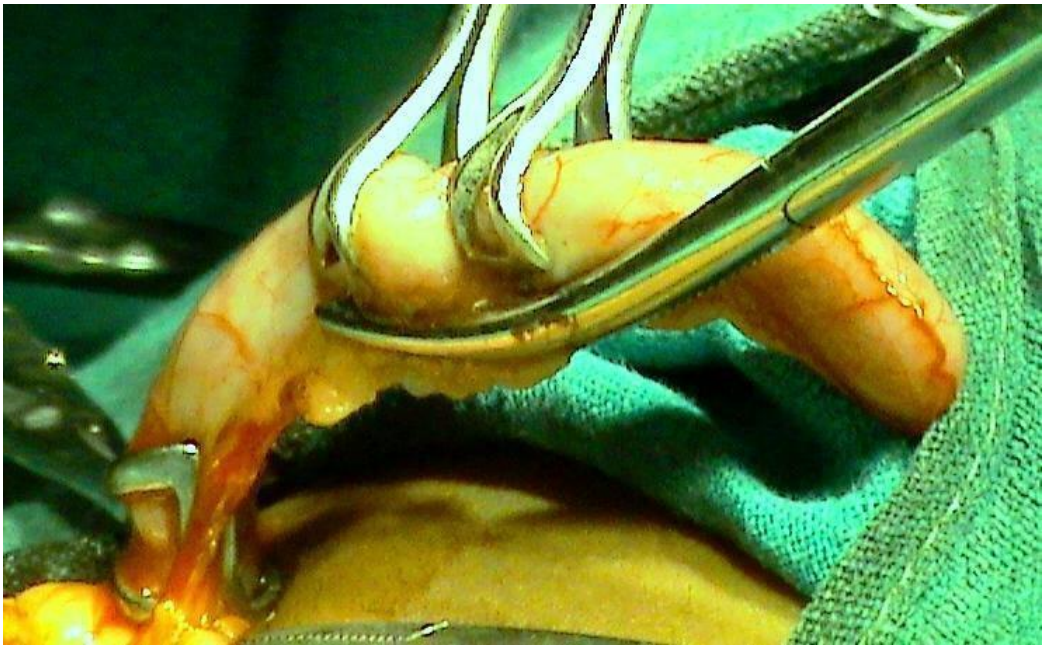
CONCLUSION

The present study suggests-

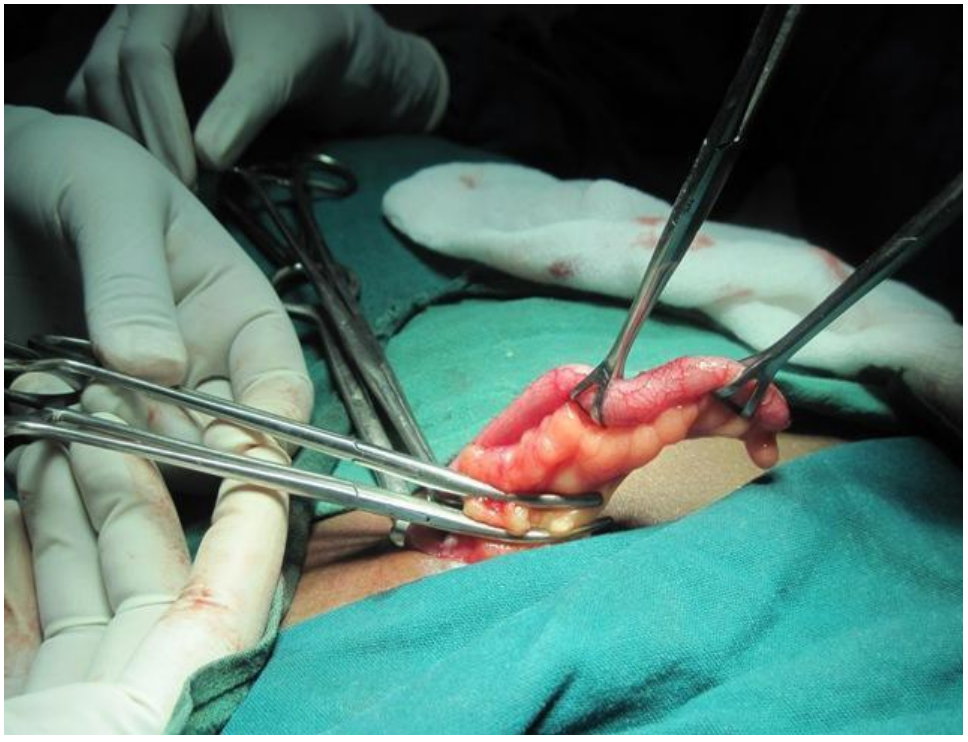
- Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis remains essentially still - clinical. Its level come out to be a credible *aid* in diagnosis of acute appendicitis and would be helpful investigation in decision making.

- Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia higher than the normal range should be identified as having a higher probability of Appendicular perforation suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

PHOTOGRAPHS

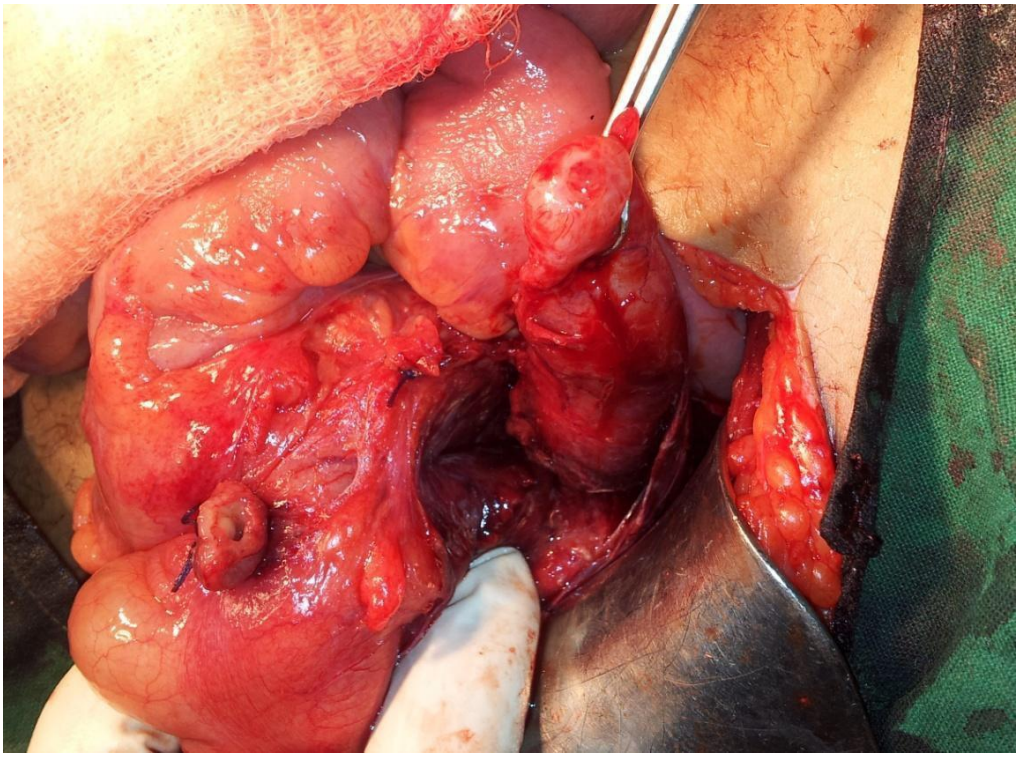


Photograph 1: Acute Appendicitis



Photograph 2. Acute appendicitis (meso appendix being ligated)

Photograph 3: Inflamed Appendix with Faecalith



Photograph 4: Appendicular perforation (ligated and cut at base)

SUMMARY

Acute appendicitis is the most common cause of “acute abdomen” in young adults. Diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations. Importance of hyperbilirubinemia or elevated Serum Bilirubin and its association in acute appendicitis has been postulated recently. It is hypothesized that an association exists between hyperbilirubinemia and acute appendicitis and its complications.

The present study was undertaken to assess relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to see whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

The present study was conducted in the Department of Surgery, GRH & MMC Madurai during the period of August 2017 to August 2018. A total of 100 patients with clinical diagnosis of acute appendicitis or Appendicular perforation

were studied. The serum bilirubin and LFTs were carried out in all the patients.

In this study, males (56%) outnumbered females (44%) and overall the mean age was 23.1 ± 11.99 years. Mean total bilirubin was noted as 1.5 ± 0.8 mg/dL (range, 0.7 – 2.3 mg/dL) while direct bilirubin was 1.0 ± 0.7 mg/dL (0.2- 1.7 mg/dL). The mean SGOT and SGPT were 27.9 ± 12.2 U/L (range, 15.7-40.1U/L) and 25.9 ± 11.0 U/L (range, 14.9 35.9U/L).

The mean ALP values were 80.8 ± 21.6 U/L (range, 59.2 -102.4 U/L).

Normal bilirubin values were seen in 26% patients while, 74% had raised bilirubin levels (Hyperbilirubinemia). Of 81 patients with acute appendicitis, 71.6% had raised bilirubin levels, while 28.4% had normal levels. 19 patients were diagnosed as Appendicular perforation, 16 patients (84.21%) had raised bilirubin levels, while the remaining 03 patients (15.79%) had normal levels. The total leukocyte count was less than 11,000/mm^3 in 65% patients while, 35% patients had counts above 11,000/mm^3.

Of the 100 patients, 91% were diagnosed as acute appendicitis clinically while 9% were diagnosed with Appendicular perforation. On Ultrasonography, 82% patients were diagnosed with acute appendicitis or appendicular perforation while 18% had normal findings. Post-operatively 81% were confirmed as acute appendicitis while 19% were diagnosed with Appendicular perforation.

The mean bilirubin levels in patients diagnosed with acute appendicitis was 1.4 ±0.65 mg/dL (range, 0.75 – 2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.9±1.16 mg/dL (range, 0.74 – 3.06 mg/dL). The Direct bilirubin and Indirect bilirubin in patients diagnosed with acute appendicitis was 0.9±0.57 mg/dL and 0.5±0.21 respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with Appendicular perforation was 1.2±1.06 mg/dL and 0.70±0.33 mg/dL respectively.

58 patients (71.6%) of the total patients diagnosed with acute appendicitis (n=81) were found to have elevated bilirubin levels while 23 patients (28.4%) had normal bilirubin levels. Similarly, 16 patients (84.21%) of the total patients diagnosed with Appendicular perforation (n=19) were found to have elevated bilirubin levels while 03 patients (15.79%) had normal bilirubin levels.

The Sensitivity and Specificity of serum bilirubin as a marker in predicting acute appendicitis and Appendicular perforation was 71.6% and 15.79% respectively. Similarly the Positive predicative value and Negative predicative value for the same was 78.38% and 11.54% respectively with odds ratio 0.472.

Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis is essentially still - clinical. Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia double the normal range (Raise in Direct Bilirubin being still higher) should be identified as having a higher probability of Appendicular perforation suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

BIBLIOGRAPHY

1. O' Connel PR. “The Vermiform Appendix”. In: Williams NS, Bulstrode CJK, O'Connell PR (Ed.). Bailey and Love's - Short practice of surgery. 25 ed. London: Arnold: 2008; p. 1204-8.

2. Smink DS, Soybel DI. “Appendix and Appendectomy”. In: Zinner MJ, Stanely W (eds) Maingot"s abdominal operations. 11th ed. Ashely: McGraw Hill; 2007. p. 589-612.

3. *John Maa. “The Appendix”. In Townsend CM,* Beauchamp RD, Evers BM, Mattox KL, eds. *Sabiston Textbook of Surgery. 18th ed.* Philadelphia, Pa: Saunders Elsevier; 2008. p: 1333-1347.

4. Deutsch A, Shani N, Reiss R. Are some appendectomies unnecessary: an analysis of 319 white appendices. J R Coll Surg Edinb 1983; 28: 35-40.

5. Piper R, Kager E, Nasman P. Acute appendicitis a clinical study of 1018 cases of emergency appendicectomy. Acta Chir Scand. 1982; 148:51-62.

6. Von von Titte SN, Mc Cabe CJ, Ottinger LW. Delayed appendicectomy for appendicitis causes and consequences. Am J Emerg Med.
1996;14:620.

7. Temple CL, Huchcroft SA, Temple WJS. Natural History of appendicitis in adult: A prospectivestudy. Ann Surg. 1995; 221: 78.

8. *Grönroos JM, Grönroos P.* A fertile-aged woman with right lower abdominal pain but unelevated leukocyte count and C-reactive protein: acute appendicitis is very unlikely. Langenbecks Arch Surg 1999*;* 384*:*
437-*40.*

9. *Jeffrey RB, Laing FC, Lewis FR.* Acute appendicitis: high-resolution real- time US findings. Radiology 1987*;* 163*:* 11-*4.*

10. *Puylaert JBCM, Rutgers PH, Lalisang RI,* de Vries BC, van der Werf SD, Dörr JP, *et al.* A prospective study of ultrasonography in the diagnosis of appendicitis. N Engl J Med 1987*;* 317*:* 666-*9.*

11. *Rioux M.* Sonographic detection of the normal and abnormal appendix. AJR Am J Roentgenol 1992*;* 158*:* 773-*8.*

12.*Lim HK, Lee WJ, Lee SJ, Namgung S, Lim JH.* Focal appendicitis confined to the tip: diagnosis at US. Radiology 1996*;* 200*:* 799-*801*.

13. Alvarado A. A practical score for early diagnosis of acute appendicitis. Ann Emerg Med 1986; 15: 557-64.

14.Kalan M, Tabbot O, Cunlife WJ, Rich AJ. Evaluation of the modified Alvrado score in the diagnosis of acute appendicitis. A prospective study. Ann R Cool Surg Engl 1994; 76: 418-9.

15.Khan S. Evaluation of hyperbilirubinemia in acute inflammation of appendix: A prospective study of 45 cases. KUMJ 2006; 4(3) 15: 281-9.

16.Beg RB, Garlungton AW. Translocation of certain endogenous bacteria from the GI tract to mesenteric lymph node and other organ in Gonobiotic mouse model. Infect Immunol 1979; 23: 403-11.

17. Juric I, Primorac D, Zagar Z, Biocic M, Pavić S, Furlan D, et al. Frequency of portal and systemic bacteremia in acute appendicitis. Pediatr Int 2001; 43(2): 152-6.

18. Koito Scathen WE, Desprez JD and Holden WD. A bacteriologic study in portal blood in man. Arch Surg 1995; 71: 404-9.

19. Wang P, Ayala A, Ba ZF, Zhou M, Perrin MM, Chaudry IH. Tumor necrosis factor –alpha produces hepatocellular dysfunction despite of normal cardiac output and hepatic microcirculation. Am J Physiol Gastrointet Liver Physiol 1993: 265(1): 126-32.

20. Wang P, Ba ZF, Chaudhary IH. Hepatic extraction of indo-cyanine green is depressed in early sepsis despite increase hepatic blood flow and cardiac output. Arch Surg 1991; 126(2):219-24.

21. Wang P, Chudhary IH. Mechanism of hepatocellular dysfunction during hyper dynamic sepsis. Am J Physiol Regul Integr Comp Physiol 1996;

270: 927-38 and 363-61.

22. Whiting JF, Green RM, Rosen AB, Gollan JL. TNF-alpha decreases hepatocyte bile salt uptake and mediated endotoxin-induced cholestasis. Hepatology. 1995; 22(4 Pt 1): 1273-8.

23. Bernard M. Jaffe and David H. Berger. “The Appendix”. In Brunicardi F, Andersen D, Billiar T, Dunn D, Hunter J, Matthews J, et al. Schwartz's Principles of Surgery. 9th ed. New York: McGraw Hill; 2009. p.1073-1092.

24. Wolff H. Medical history aspects of appendicitis treatment. Zentralbl Chir 1998; 123 Suppl 4: 2-5.

25. Reith HB. Appendizitis and Perityphilitis: Historischer Überblick. Chir Gastroenterol 1993; 9: 184-96.

26. Fitz RH. Perforating inflammation of the vermiform appendix, with special reference to its early diagnosis and treatment. Trans Ass Amer Phys 1886; 1: 107–44.

27. D`Alia C, Lo Schiavo MG, Tonante A, Taranto F, Gagliano E, Bonanno L, et al. Amyand"s hernia: case report and review of the literature. Hernia 2003; 7: 89-91.

28. McBurney C. The Incision Made in the Abdominal Wall in Cases of Appendicitis with a Description of a New Method of Operating. Ann Surg 1894; 20(1): 38-43.

29. Gordon RC. John B. Murphy: unique among American surgeons. J Invest Surg 2006; 19: 279-81.

30. Litynski GS. Kurt Semm and the fight against skepticism: endoscopic hemostasis, laparoscopic appendectomy, and Semm"s impact on the "laparoscopic revolution". JSLS 1998; 2: 309-13.

31. Inderbir Singh, GP Pal. Human embryology. Macmillan Publishers India Limited, Chennai. 6th edition: 2007: p. 155

32. Jeremiah C Healy. “Vermiform appendix”. Chapter 78. In Grays anatomy – The anatomical basis of clinical practice. 39th edition. Churchill Livingstone. Susan Standring Elsevier: 2005; p. 1189-90.

33. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol 1990; 132 (5): 910-25.

34. Flum DR, Morris A, Koepsell T, Dellinger EP. Has misdiagnosis of appendicitis decreased over time? A population-based analysis. JAMA 2001; 286 (14): 1748-53.

35. Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: Nationwide analysis. Arch Surg. 2002; 137(7): 799-804.

36. Burkitt DP. The aetiology of appendicitis. Br J Surg 58: 695: 1971

37. Boyd W. Pathology for surgeons. Philadelphia: WB Saunders; 8th edition:1996.

38. Rautio M, Saxen H, Siitonen A, Nikku R, Jousimies-Somer H. Bacteriology of histopathologically defined appendicitis in children. Pediatr Infect Dis J 2000; 19: 1078-83.

39. Allo MD, Bennion RS, Kathir K, Thompson JE Jr, Lentz M, Meute M, et al: Ticarcillin/clavulanate versus imipenem/cilastatin for the treatment of infections associated with gangrenous and perforated appendicitis. Am Surg 1999; 65: 99-104.

40. Soffer D, Zait S, Klausner J, Kluger Y. Peritoneal cultures and antibiotic treatment in patients with perforated appendicitis. Eur J Surg 2001; 167: 214-6.

41. Kokoska ER, Silen ML, Tracy TF Jr., Dillon PA, Kennedy DJ, Cradock TV, et al. The impact of intraoperative culture on treatment and outcome in children with perforated appendicitis. J Pediatr Surg. 1999; 34(5): 749-53.

42. Bhajekar M.V.: Surgical Appendix. In Indian journal of Medical Sciences, Bombay: 1963.

43. Kenneth S. Latchis, Jerome W. Canter. Acute appendicitis secondary to metastatic carcinoma. American journal of surgery, 1966: 111(2): 220-223.

44. S N De, K P Sengupta. The amoebic appendix and its perforation. J Indian Med Assoc., 1952: 21(6): 242-245.

45. Marudanayagam R, Williams GT, Rees BI. Review of the pathological results of 2660 appendicectomy specimens. J Gastroenterol 2006; 41: 745-9.

46. Thompson MM, Underwood MJ, Dookeran KA, Lloyd DM, Bell PRF. Role of sequential leucocyte counts and C-reactive protein measurements in acute appendicitis. Br J Surg; 1992; 79: 822-4.

47. Thimsen DA, Tong GK, Gruenberg JC. Prospective evaluation of C- reactive protein in patients suspected to have acute appendicitis. *Am Surg* 1989; 55(7): 466-8.

48. de Carvalho BR, Diogo-Filho A, Fernandes C, Barra CB. Leukocyte count, C reactive protein, alpha-1 acid glycoprotein and erythrocyte sedimentation rate in acute appendicitis. *Arq Gastroenterol* 2003; 40(1): 25-30.

49. Albu E, Miller BM, Choi Y, et al. Diagnostic value of C-reactive protein in acute appendicitis. *Dis Colon Rectum.* 1994; 37(1): 49-51.

50. Gurleyik E, Gurleyik G, Unalmiser S. Accuracy of serum C-reactive protein measurements in diagnosis of acute appendicitis compared with surgeon's clinical impression. *Dis Colon Rectum* 1995; 38(12): 1270-4.

51. Wise SW, Labuski MR, Kasales CJ, Blebea JS, Meilstrup JW, Holley GP, et al. Comparative assessment of CT and sonographic techniques for ap- pendiceal imaging. AJR Am J Roentgenol 2001; 176: 933-41.

52. Rao PM, Rhea JT, Novelline RA, Mostafavi AA, McCabe CJ. Effect of computed tomography of the appendix on treatment of patients and use of hospital resources. N Engl J Med 1998; 338: 141-6.

53. Weltman DI, Yu J, Krumenacker J, et al. Diagnosis of acute appendicitis: Comparison of 5- and 10-mm CT sections in the same patient. Radiology 2000; 216: 172-7.

54. Estrada JJ, Petrosyan M, Krumenacker J Jr, Huang S, Moh P. Hyperbilirubinemia in Appendicitis: A New Predicator of Perforation. Journal of Gastrointestinal Surgery 2007; 11: 714–5.

55. Berk PD, Wolkoff AW. Bilirubin Metabolism and Hyperbilirubinemia. In: Kasper DL, Braunwald Braunwald E, *Fauci* AS, Hauser SL, Longo DL, Jameson JL, et al. Harrison‟s Textbook of Internal Medicine. 16th ed. Vol. II. New York: McGraw Hill Medical Publishing Division; 2001. p. 919
.

56. William C, Mayers, MD., Rocco Ricciardi, MD. Liver Function. In: *Townsend CM,* Beauchamp RD, Evers BM, Mattox KL, eds. Sabiston Text Book of Surgery. The biological basis of modern surgical practice, Book-I. 11th ed. A Heart Court Asia PTE LTD; 2001. p.1010.

57. Sherlock S, Dooley J. Assessment of Liver Function. In: Liver and hepatobiliary Diseases. 11th Ed. Oxford: Black Well Publishing Company; 2002. p 20.

58. Kevin p. Lally, MD, Charles S. Cox Jr., MD, Richard J Andressy MD. Appendix. In: *Townsend CM,* Beauchamp RD, Evers BM, Mattox KL, eds. Sabiston Text Book of Surgery. The biological basis of modern surgical practice, Book-I. 11th ed. A Heart Court Asia PTE LTD; 2001. p. 917.

59. Chand N, Sanyal AJ. Sepsis induced cholestasis. J Hepatol 2007; 45: 203- 41.

60. Geier A, Fickert P, Trauner M. Mechanisms of disease: mechanismand clinical implications of cholestasis in sepsis. Nat Clin Pract Gastroenterol Hepatol 2006; 3: 574-85.

61. Baron EJ, Bennion RS, Thompson JE, Strong C, Summanen P, McTeague M, et al. A microbial comparison between acute appendicitis and complicated appendicitis. Clin Infect Dis 1992; 14: 227-31.

62. Rink RD, Kaelin CR, Giammara B, Fry DE. Effects of live Escheria Coli and bacteroids fragilis on metabolism and hepatic pO2. Circ Shock 1981; 8: 601-11.

63. Green RM, Beier D, Gollan JL. Regulation of hepatocyte bile salt transporters by endotoxin and inflammatory cytokines in rodents. Gastroenterology 1976; 111: 193-8

64. Utili R, Abernathy CO, Zimmerman HJ. Cholestatic effects of Escheria Coli endotoxin on isolated perfused rat liver. Gastroenterology 1976; 70: 248-53.

65. Shander A. Anemia in critically ill. Crit Care Clin 2004; 20: 159-78.

66. Agrez MV, House AK, Quinlan MF. Jaundice may herald an appendiceal abscess. Aust N Z J Surg 1986; 56: 511-3.

67. Seller RA. Jaundice in acute appendicitis. Lancet 1969; 1: 838.

68. Sand M, Bechara GF, Holland-Letz T, Sand D, Mehnert G, Mann B. Diagnostic value of Hyperbilirubinemia as a predictive factor for Appendiceal perforation in Acute Appendicitis. Am J Surg 2009 Aug;198(2):193-8

69. Emmanuel A, Murchan P, Wilson I, Balfe P. The value of hyperbilirubinaemia in the diagnosis of acute appendicitis. Ann R Coll Surg Engl 2011; 93(3): 213-7.

70. Khan S. Elevated serum Bilirubin in Acute Appendicitis: a new Diagnostic tool. Kathmandu University Medical Journal 2008; 6 (2): 161-5.

71. Kasper DL, Braunwald Braunwald E, *Fauci* AS, Hauser SL, Longo DL, Jameson JL, et al. Harrison‟s Principles of Internal Medicine. 16th ed. McGraw Hill; 2005.

72. The appendix. In: Decker GAG, Plessis, du DJ. Lee McGregror‟s Synopsis of surgical anatomy. Bristol: Varghese Publishing House; 1986; (12): 31-42.

73. Crawford JM. Appendix. In: Kumar V (Eds). Robbins and Cotran - Pathologic basis of disease. Philadelphia, Pensylvania: Elsevier; 2004. p.
870-1.

74. Livingston EH, Woodward WA, Sarosi GA, Haley RW. Disconnect between incidence of nonperforated and perforated appendicitis: Implications for pathophysiology and management. Ann Surg. 2007;
245(6): 886-92.

ANNEXURES

Informed Consent

Name: Age/ Sex: IP:

I herewith declare that I have been explained in a language fully understood by me regarding the purpose of this study, methodology, proposed intervention, plausible side effects, if any and sequelae.

I have been given an opportunity to discuss my doubts and I have received the appropriate explanation.

I understand that my participation in this study is completely voluntary and that I am free to withdraw from this study at anytime without any prior notice &/ or without having my medical or legal rights affected.

I permit the author and the research team full access to all my records at any point, even if I have withdrawn from the study. However my identity will not be revealed to any third party or publication.

I herewith permit the author and the research team to use the results and conclusions arising from this study for any academic purpose, including but not limited to dissertation/ thesis or publication or presentation in any level.

Therefore, in my full conscience, I give consent to be included in the study and to undergo any investigation or any intervention therein.

Patient's Sign Investigator's Sign

(Dr.SANJU UNNIKRISHNAN)

"**A COMPARATIVE STUDY OF DIAGNOSTIC VALUE OF HYPERBILIRUBINEMIA IN PREDICTING APPENDICITIS AND ITS COMPLICATIONS"**

Investigator: **Dr.SANJU UNNIKRISHNAN** , PGY3 – MS (Gen Surg)

Guide: **Prof. Dr.P. AMUTHA** MS

- NAME : SL. NO:
- AGE /SEX:
- ADDRESS WITH CONTACT NUMBER:
- IP NO:
- DATE OF ADMISSION:
- DATE OF SURGERY:

:

HISTORY OF PRESENTING ILLNESS:

Pain :

duration ,

location ,

character

Vomiting:

onset :

duration:

Nausea

Anorexia

Fever

Diarrhoea

Any other relevant history

PAST HISTORY:

whether a known case of dm/hypertension/asthma/tb/epilepsy/cardiac illness

H/O jaundice/liver disease/hemolytic disorders

GENERAL EXAMINATION:

TEMP:

P.R:

B.P:

R.R

SYSTEMIC EXAMINATION:

CVS

RS

PER ABDOMEN:

PER RECTAL

CLINICAL DIAGNOSIS:

Investigations:

HEMAT		**LFT**	
HB		T.BIL	
PCV		D.BIL	
RBC			
TC			
DC			
PLT			
ESR			
RBS & ELECTROLYTE			

CHEST X RAY :

ABD X RAY:

USG ABD:

PATIENT CLINICAL COURSE:

OUTCOME OF TREATMENT:

Information Module

You are being invited to be a subject in this study.

Before you participate in this study, I am giving you the following details about this trial, which includes the aims, methodology, intervention, possible side effects, if any and outcomes:

All patients diagnosed with acute appendicitis on clinical examination and imaging will be included in this study. A detailed clinical history will be taken following a standardized proforma. A detailed clinical examination will be made and relevant investigations, basic and special investigations will be done at the time of admission.Bilirubin level and USG abdomen will be done at the time of admission. The prevalence of hyperbilirubinemia in acute appendicitis will be analysed. The results arising from this study will be analyzed and use for academic purposes. You will be given clear instructions at every step and you are free to ask/ clarify any doubts. Your identity will remain confidential. You are free to withdraw from this trial at any point of time, without any prior notice &/ or without any medical or legal implications.

I request you to volunteer for this study.

Thanking You,

(Dr.SANJU UNNIKRISHNAN) Name:

Serial Number	NAME	In Patient (IP) Number	Gender	Age	Liver function tests						TLC (/cumm3)	DLC				Clinical Diagnosis on	Ultra - Sonogra	Per-	Post-
					Total Biliru	Direct Biliru	Indirect	SGOT	SGPT	ALP		Neutrop	Lymphoc	Eosinoph	Monocyt				
1	Sathis	1450365	M	14	0.6	0.3	0.3	46	13	112	14300	89	7	4	0	AA	AA	AA	A
2	Ravi	26035	M	27	1.1	0.4	0.7	22	43	83	8200	75	20	2	3	AA	N	AA	A
3	Sullu	26098	M	22	0.8	0.2	0.6	91	26	100	9900	85	7	6	2	AA	AA	AA	A
4	Sivasankari	1448142	F	27	1.2	0.8	0.4	16	26	56	12200	57	40	3	0	AA	AA	AA	A
5	Venketesan	144810	M	29	1.4	0.9	0.5	35	12	93	6700	63	27	8	2	AA	AA	AA	A
6	Veeraragavan	260534	M	28	2.9	2.2	0.7	46	22	106	9300	87	12	1	0	AP	N	AP	A
7	Rajalakshimi	1448209	F	32	1.2	0.8	0.4	12	24	110	10900	64	28	6	2	AA	AA	AA	A
8	Sathya	1448207	F	14	1.4	1.2	0.2	34	12	76	8600	66	24	6	4	AA	AA	AA	A
9	Kalaiselvi	1448212	F	15	1.5	1.1	0.4	38	12	117	12300	78	13	7	2	AA	AA	AA	A
10	Shanawash	1448060	M	13	1.4	1.0	0.4	10	35	22	6300	58	40	2	0	AA	N	AA	A
11	Vanitha	1448240	F	16	4.4	3.4	1.0	25	39	54	10500	86	12	1	1	AA	AP	AP	A
12	Arun	1444007	M	18	0.8	0.2	0.6	34	29	92	2300	58	32	7	3	AA	AA	AA	A
13	Kowsalya	1448869	F	30	1.1	0.7	0.4	34	26	78	8600	55	42	2	1	AP	AA	AP	A
14	Senthil	1448209	M	29	0.9	0	1	18	16	45	14100	90	8	2	0	AA	AA	AA	A
15	Manimaran	1442977	M	20	0.9	0.2	0.7	32	11	77	7400	59	37	4	0	AA	AA	AA	A
16	Ganesan	20952	M	39	1.6	1.2	0.4	29	17	74	14200	85	13	2	0	AA	AA	AP	A
17	Jeejibai	20903	F	24	1.7	1.3	0.4	25	25	29	6900	71	29	0	0	AA	AA	AA	A
18	Kalaiarasan	21051	M	14	1.3	1.1	0.2	38	29	81	8100	54	44	1	1	AA	AP	AP	A
19	Shylash	21046	M	27	0.9	0.3	0.6	24	23	100	9900	58	40	2	0	AA	N	AA	A
20	Lalitha	20929	F	14	3.2	2.5	0.7	14	15	59	15500	80	18	2	0	AP	AP	AP	A
21	Saranya	21024	F	23	1.0	0.3	0.7	29	31	94	8200	50	47	2	1	AA	AA	AP	A
22	Shanthi	21222	F	40	1.4	1.2	0.2	33	11	72	9900	80	18	2	0	AA	AA	AA	A
23	Manjula	22114	F	17	1.2	0.3	0.9	25	14	67	12400	66	30	1	3	AA	AA	AA	A
24	Thangamani	21798	F	17	0.6	0.5	0.1	40	29	81	9500	60	30	#	0	AA	N	AA	A
25	Manjula	22114	F	18	1.4	1.1	0.3	34	12	81	12700	86	8	5	1	AA	N	AA	A
26	Usha	21983	F	11	1.6	1.2	0.4	19	22	71	10400	60	40	0	0	AA	AA	AA	A
27	Arunkumar	21983	M	16	4.2	3.8	0.4	22	12	80	12500	64	26	6	4	AP	AP	AP	A
28	Balaji	22035	M	22	1.3	0.9	0.4	34	12	96	4400	76	18	4	2	AA	N	AA	A
29	Kodiswaren	22071	M	27	1.1	0.8	0.3	22	34	30	10000	68	30	1	1	AA	AA	AA	A
30	Pushparaj	22104	M	45	0.6	0.3	0.3	18	18	98	16700	65	25	8	2	AP	AP	AP	A
31	Mani	20227	M	30	2.8	2.1	0.7	26	33	68	13300	74	20	4	2	AP	AP	AP	A
32	Maragatham	21957	F	25	2.0	1.2	0.8	30	94	130	9860	88	11	1	0	AA	AA	AP	A
33	Suryakumari	22065	F	41	1.4	0.7	0.7	30	48	110	11300	85	10	4	1	AA	AA	AA	A
34	Thyagu	22108	M	25	0.8	0.3	0.5	38	44	120	10250	65	30	5	0	AA	AA	AA	A
35	Valli	22896	F	23	0.9	0.4	0.5	18	34	44	14000	80	18	1	1	AA	AA	AA	A
36	Uma	1443143	F	10	2.3	1.5	0.8	24	32	100	4800	55	40	3	2	AA	AA	AP	A
37	Jothi	22036	F	25	1.1	0.6	0.5	27	22	65	9800	45	50	5	0	AA	N	AA	A

38	Nadhiya	23400	F	14	1.4	0.8	0.6	22	32	56	12000	88	10	1	1	AA	N	AA	AA
39	Ganesan	23141	M	10	1.0	0.3	0.7	25	34	70	2300	80	20	0	0	AA	AA	AA	AA
40	Nasrin	20600	F	17	1.4	1.0	0.4	32	14	56	15400	76	22	3	1	AA	AA	AA	AA
41	Jasmin	23185	F	25	0.7	0.5	0.2	24	20	92	16700	65	25	8	2	AA	AA	AA	AA
42	Kuppan	23155	M	16	2.8	2.1	0.7	26	33	68	13300	80	15	4	1	AA	AA	AA	AA
43	Venketesan	22870	M	26	2.0	1.4	0.6	12	15	110	9800	88	11	1	0	AA	N	AA	AA
44	Manjula	23368	M	30	0.7	0.4	0.3	34	18	90	11300	85	10	4	1	AA	N	AA	AA
45	Murugavalli	22577	F	18	1.7	1.2	0.5	31	12	90	10250	65	30	5	0	AA	AA	AA	AA
46	Ravi	26085	M	38	1.4	0.4	1.0	35	28	90	14000	80	18	1	1	AA	AP	AP	AP
47	Ganesan	26112	M	45	2.2	0.8	1.4	40	38	90	14800	85	10	3	2	AA	AP	AP	AP
48	Sillu	26098	M	35	1.1	0.6	0.5	27	22	65	9800	45	50	5	0	AA	AP	AP	AP
49	Durai	26002	M	12	0.9	0.2	0.7	15	22	110	12000	88	10	1	1	AP	AP	AP	AP
50	Mari	14272280	M	35	1.0	0.3	0.7	25	34	70	2300	80	20	0	0	AA	AA	AA	AA
51	Samantha rani	25798	F	28	1.4	1.0	0.4	32	14	56	15400	76	20	3	1	AA	AA	AA	AA
52	Raman	27007	M	13	1.6	1.4	0.2	38	27	86	5000	60	38	2	0	AA	AA	AA	AA
53	Rasith	27253	M	33	2.5	2.2	0.3	21	33	45	11200	77	13	7	3	AA	AA	AA	AA
54	Shyla	26039	F	60	0.8	0.6	0.2	32	13	55	8400	78	20	1	1	AA	N	AA	AA
55	Suganthi	25098	F	18	1.1	0.9	0.2	12	33	80	12800	50	40	9	1	AA	AA	AA	AA
56	Madheena beevi	25974	F	13	2.1	1.5	0.6	35	25	90	7500	80	20	0	0	AA	AA	AA	AA
57	Chandra	27293	F	25	0.7	0.5	0.2	28	32	80	3500	65	30	5	0	AA	AA	AA	AA
58	Lakshimi	27452	F	28	3.2	2.0	1.2	29	21	33	18000	70	28	1	1	AA	N	AA	AA
59	Shalini	27650	F	15	1.4	0.9	0.5	26	24	65	9800	80	18	1	1	AA	AA	AA	AA
60	Uma maheshwari	27379	F	20	1.9	1.3	0.6	34	34	98	11000	60	30	8	2	AA	AA	AA	AA
61	Kishore kumar	27281	M	28	1.8	1.2	0.6	40	29	87	6700	65	35	0	0	AA	N	AA	AA
62	Sathiskumar	28978	M	20	1.2	1.0	0.2	25	35	65	9900	88	10	2	0	AA	AA	AA	AA
63	Prasanth	29680	M	60	1.2	0.6	0.6	19	21	47	6750	80	16	3	1	AA	AA	AA	AA
64	Suresh	29198	M	12	1.3	0.9	0.4	33	24	88	12000	78	20	2	0	AP	AP	AP	AP
65	Sakthivel	29227	M	9	1.5	0.6	0.9	20	13	24	6700	60	38	1	1	AA	AA	AA	AA
66	Shyamala	27342	F	22	1.6	1.0	0.6	35	34	65	3400	50	46	4	0	AA	N	AA	AA
67	Rekha	29140	F	12	2.0	1.2	0.8	16	34	120	18450	70	22	6	2	AA	AA	AA	AA
68	Mohammed rafi	29207	M	55	1.9	1.3	0.6	34	28	45	5600	66	30	4	0	AA	AA	AA	AA
69	Suresh kumar	29210	M	20	3.5	2.7	0.8	33	55	78	22540	78	21	1	0	AA	AA	AA	AA
70	Udhayakumari	29234	F	35	1.5	1.2	0.3	23	34	67	7500	60	30	8	2	AA	AA	AA	AA
71	Arumugam	29088	M	17	1.1	0.6	0.5	12	23	56	9000	75	20	2	3	AA	N	AA	AA
72	Silambarasan	29223	M	8	1.3	0.9	0.4	21	34	46	8000	67	30	3	0	AA	AA	AA	AA
73	Aravind	28646	M	13	1.4	1.0	0.4	14	14	76	7600	78	22	0	0	AA	AA	AA	AA
74	Prasanna	28826	M	30	0.8	0.6	0.2	32	21	64	9000	50	40	#	0	AA	AA	AA	AA
75	Anand	28535	M	28	1.7	0.7	1.0	34	34	76	8500	80	18	2	0	AA	AA	AA	AA
76	Nagaraj	28968	M	38	0.6	0.5	0.1	34	23	76	10500	76	20	3	1	AA	AA	AA	AA
77	Sangeetha	28931	F	30	1.4	1.2	0.2	22	32	48	7000	55	35	8	2	AA	N	AA	AA
78	Raja	28976	M	21	2.9	2.0	0.9	25	32	88	13100	68	30	0	2	AA	AA	AA	AA

79	Babu	1441436	M	8	3.9	3.0	0.9	26	13	132	9000	80	16	4	0	AA	AA	AA	A
80	Sasi	1441420	M	20	2.3	1.6	0.7	21	19	100	14500	82	16	1	1	AA	AA	AA	A
81	Karthick	1441460	M	18	0.9	0.2	1	20	23	106	4800	67	20	3	0	AA	AA	AA	A
82	Revathi	1441465	F	22	1.2	0.2	1	12	22	89	6400	83	10	5	2	AA	AP	AP	A
83	Chellamma	1441463	F	70	1.3	0.9	0	10	10	113	13800	88	8	2	2	AA	AA	AA	A
84	Chandru	1443257	M	15	0.9	0.3	1	23	21	67	4400	80	12	6	2	AA	AA	AA	A
85	Manikandan	1445064	M	32	1.3	1.1	0	24	32	99	8000	67	29	3	1	AA	AA	AA	A
86	Vijay	1443879	M	18	1.6	1.2	0	12	34	110	9400	80	12	6	2	AA	AA	AA	AA
87	Narain	1443865	M	20	1.8	1.3	0.5	22	35	100	8300	58	29	9	4	AA	AA	AA	A
88	Saravanan	1443783	M	19	0.6	0.2	0.4	18	17	110	8600	64	30	5	1	AA	N	AA	A
89	Rameshkumar	1443663	M	26	1.4	1.2	0.2	32	25	111	15000	90	6	3	1	AA	AA	AA	A
90	Keerthivasan	1443628	M	12	1.3	0.5	0.8	26	39	91	4500	69	27	4	1	AP	AP	AP	A
91	Saraswathi	1441462	F	12	1.7	1.2	0.5	19	25	56	6900	63	32	4	1	AA	AA	AA	A
92	Saroja	1441549	F	28	0.9	0.3	0.6	34	46	120	14300	89	7	4	0	AA	AA	AA	A
93	Shathi	1441550	F	15	1.1	0.4	0.7	22	43	83	8200	75	20	5	0	AA	AA	AA	A
94	Farook	1445893	M	16	0.8	0.2	0.6	91	26	100	9900	85	7	6	2	AA	AA	AA	A
95	Madhavan	1443891	M	11	1.2	0.8	0.4	16	26	56	12200	57	40	2	1	AA	AA	AA	A
96	Priyanka	1441492	F	12	1.4	0.9	0.5	35	12	93	6700	63	29	8	0	AA	AA	AA	AA
97	Geetha	1444293	F	10	0.9	0.2	0.7	46	22	106	9300	87	12	1	0	AA	AA	AA	A
98	Gunasekaran	1443973	M	21	2.2	1.8	0.4	12	24	110	10000	64	28	6	2	AA	AA	AA	A
99	Soundarya	1444009	F	14	1.4	1.2	0.2	34	12	76	8600	66	27	5	2	AA	AA	AA	A
100	Vijayarai	1444151	M	24	1.5	1.1	0.4	38	12	117	12500	78	14	6	2	AA	AA	AA	A

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University,
Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.Sanju Unnikrishnan
Course	:	PG in MS., General Surgery
Period of Study	:	2016-2019
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	A comparative study of diagnostic value of hyperbilirubinemia in predicting appendicitis and its complications
Ethical Committee as on	:	31.03.2018

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary Chairman Dean / Convenor

Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
Professor Emeritus Neuroscience
Sr. Consultant Neurologist
Director, VN Neuro Care Centre
Madurai-625 001

Madurai Medical College
Madurai-20

19 JUN 2018

KEY TO MASTER CHART

AA - Acute appendicitis

ALP - Alkaline phosphatase

AP - Appendicular perforation

dL - Deciliters

DLC - Differential leukocyte count

F - Female

M - Male

mg - Milligrams

mm - Millimeters

N - Normal

SGOT - Serum glutamic oxaloacetic transaminase

SGPT - Serum glutamic pyruvic transaminase

TLC - Total leukocyte count

URKUND

Urkund Analysis Result

Analysed Document: Final Thesis.pdf (D42118713)
Submitted: 10/4/2018 12:25:00 PM
Submitted By: sanju89rulz@gmail.com
Significance: 4 %

Sources included in the report:

Thesis word priliminary.docx (D31201225)

Instances where selected sources appear:

20

CERTIFICATE – II

This is to certify that this dissertation work titled **"A COMPARATIVE STUDY OF DIAGNOSTIC VALUE OF HYPERBILIRUBINEMIA IN PREDICTING APPENDICITIS AND ITS COMPLICATIONS"** of the candidate **Dr. SANJU UNNIKRISHNAN** with Registration Number 221611122 for the award of MASTER DEGREE in the branch of GENERAL SURGERY. I have personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 4% of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.